

EXHIBIT 1

Protected Information - Keith T. Wilson, M.D.

1 IN THE UNITED STATES DISTRICT COURT
2 FOR THE DISTRICT OF NEW JERSEY

3 -----

4 IN RE: BENICAR MDL NO. 2606
5 (OLMESARTAN) PRODUCTS
6 LIABILITY LITIGATION

7 - - -

8 SUPERIOR COURT OF NEW JERSEY
9 LAW DIVISION - ATLANTIC COUNTY

10 -----

11 IN RE: BENICAR MCL NO. 299
12 (OLMESARTAN MEDOXOMIL)
13 LITIGATION

14 -----

15 PROTECTED INFORMATION

16

17 VIDEOTAPED EXPERT DEPOSITION OF

18 KEITH T. WILSON, MD

19 February 25, 2017

20 9:12 a.m.

21 725 12th Street NW

22 Washington, DC 20005

23

24 BY: Denise D. Vickery, CRR/RMR

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9 aslater@mskf.net	9 EXHIBITS
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<p style="text-align: right;">Page 7</p> <p>1 PROCEEDINGS</p> <p>2 - - -</p> <p>3 (Documents marked for</p> <p>4 identification purposes as Gutman</p> <p>5 Exhibit 1, Exhibit 2, Exhibit 3,</p> <p>6 Exhibit 4, and Exhibit 5.)</p> <p>7 THE VIDEOGRAPHER: We are on the</p> <p>8 record.</p> <p>9 The time now is 9:12. This marks</p> <p>10 the beginning of Disk No. 1 for the</p> <p>11 videotaped deposition testimony of</p> <p>12 Dr. Keith Wilson in the matter of Benicar</p> <p>13 Products Liability Litigation, MDL No.</p> <p>14 2606.</p> <p>15 Today's date is February 25,</p> <p>16 2017. This deposition is being conducted</p> <p>17 at 725 12th Street, Northwest,</p> <p>18 Washington, DC.</p> <p>19 Will all attorneys present please</p> <p>20 identify themselves and who they</p> <p>21 represent.</p> <p>22 MR. SLATER: Adam Slater for</p> <p>23 Plaintiffs.</p> <p>24 MS. PITTNER: Laura Pittner for</p>	<p style="text-align: right;">Page 9</p> <p>1 going to take your deposition. You understand</p> <p>2 that's what we're doing; right?</p> <p>3 A. Yes.</p> <p>4 MR. CHRISTIAN: Did you hear him?</p> <p>5 MR. SLATER: You didn't hear me?</p> <p>6 THE WITNESS: I hear you.</p> <p>7 BY MR. SLATER:</p> <p>8 Q. Did my voice cut out?</p> <p>9 A. No. Am I -- am I live?</p> <p>10 THE VIDEOGRAPHER: Yes, you're</p> <p>11 live.</p> <p>12 THE WITNESS: Yes, I heard you</p> <p>13 and I said yes.</p> <p>14 BY MR. SLATER:</p> <p>15 Q. Okay. I must have missed it.</p> <p>16 Okay. Doctor, have you been</p> <p>17 deposed before?</p> <p>18 A. Once.</p> <p>19 Q. You're under oath. Do you</p> <p>20 understand that?</p> <p>21 A. Yes.</p> <p>22 Q. Do you understand you must tell</p> <p>23 the truth and provide accurate and complete</p> <p>24 answers to every one of my questions?</p>

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<p style="text-align: right;">Page 10</p> <p>1 A. Yes.</p> <p>2 Q. If I ask you a question that</p> <p>3 doesn't make sense to you for any reason, please</p> <p>4 tell me. I'll try to rephrase it, okay?</p> <p>5 A. Yes.</p> <p>6 Q. The room may object to a</p> <p>7 question, most likely just objecting to the form,</p> <p>8 which is basically them saying I didn't ask the</p> <p>9 question the right way and they're preserving</p> <p>10 their rights to the future. Just let them say</p> <p>11 what they're going to say ask, and then I assume</p> <p>12 in most cases you're just going to answer the</p> <p>13 question, okay?</p> <p>14 A. Okay.</p> <p>15 Q. You said you were previously</p> <p>16 deposed one time.</p> <p>17 What was that in connection with?</p> <p>18 A. It was a medical malpractice</p> <p>19 case, and this was around seven years ago.</p> <p>20 Q. Were you an expert for the</p> <p>21 plaintiff or the defense?</p> <p>22 A. For the plaintiff.</p> <p>23 Q. Did it have anything to do with</p> <p>24 any sort of a malabsorption or an enteropathy</p>	<p style="text-align: right;">Page 12</p> <p>1 request number 1?</p> <p>2 A. Yes.</p> <p>3 Q. What date are those invoices</p> <p>4 current through? It says something about January</p> <p>5 2017.</p> <p>6 What was the -- is that through</p> <p>7 the end of the month all time you've spent since</p> <p>8 from the beginning to the end of January 2017?</p> <p>9 A. When you say "the month," you</p> <p>10 mean the month of January?</p> <p>11 Q. Oh, I see actually there is some</p> <p>12 February time. Let me rephrase the question.</p> <p>13 This -- these invoices look like</p> <p>14 they go through February 23, 2017.</p> <p>15 Is this all time that you've</p> <p>16 invoiced through February 23, 2017?</p> <p>17 A. So I have not invoiced the</p> <p>18 February. What the agreement that I was told was</p> <p>19 that I should at the end of each month provide a</p> <p>20 monthly invoice. So the February data is just a</p> <p>21 running Excel spreadsheet that I keep where I</p> <p>22 document what I do so that I don't forget, and I</p> <p>23 provided that yesterday, but that is not my</p> <p>24 official invoice yet because I haven't put it on</p>
<p style="text-align: right;">Page 11</p> <p>1 condition?</p> <p>2 A. No.</p> <p>3 Q. Totally unrelated to the subject</p> <p>4 matter of this case?</p> <p>5 A. Other than the fact that it was a</p> <p>6 case about a gastrointestinal issue, but not</p> <p>7 anything related to this case.</p> <p>8 Q. Okay. I have marked as</p> <p>9 Exhibit 1 -- let's give Dr. Wilson Exhibits 1, 2,</p> <p>10 3, 4, and 5 just so he has them.</p> <p>11 Okay. Exhibit 1 is the</p> <p>12 deposition notice in this case.</p> <p>13 Did you ever see the deposition</p> <p>14 notice for this deposition?</p> <p>15 A. Yes. When I met with</p> <p>16 Mr. Christian yesterday, I was shown it at that</p> <p>17 time.</p> <p>18 Q. Okay. Exhibit 2 is the response</p> <p>19 we were provided.</p> <p>20 Have you seen that document?</p> <p>21 A. No.</p> <p>22 Q. Number 1 the first request was</p> <p>23 your invoices, and if you look at Exhibit 3, is</p> <p>24 that what was -- what was provided in response to</p>	<p style="text-align: right;">Page 13</p> <p>1 my letterhead.</p> <p>2 Q. What other time would need to be</p> <p>3 added to the February worksheet, which is the</p> <p>4 last page of Exhibit 3, to make it complete?</p> <p>5 A. So I met with Randy and Neelum</p> <p>6 yesterday for approximately six hours and then</p> <p>7 whatever time we spent today, and if there will</p> <p>8 be any follow-up correspondence between now and</p> <p>9 the end of the month.</p> <p>10 Q. Let's go to the first page of</p> <p>11 Exhibit 3.</p> <p>12 How was it that you were</p> <p>13 contacted? Do you know why you were contacted in</p> <p>14 this case?</p> <p>15 A. So the initial contact was that</p> <p>16 my assistant told me that a Mr. Joseph Babington</p> <p>17 left a message, that he wanted to speak with me</p> <p>18 about a product liability case that had some</p> <p>19 relevance to gastroenterology, and she gave me</p> <p>20 his phone number. And I called him back, and we</p> <p>21 had an initial conversation in early June of</p> <p>22 2016.</p> <p>23 Q. Have you ever consulted outside</p> <p>24 of a litigation context for any pharmaceutical</p>

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<p style="text-align: right;">Page 14</p> <p>1 manufacturer?</p> <p>2 A. No.</p> <p>3 Q. Do you know why it is that</p> <p>4 Mr. Babington thought to call you as opposed to</p> <p>5 anyone else? Why? Do you know why that was?</p> <p>6 A. So of course I asked that</p> <p>7 question, and he said, "We are looking for</p> <p>8 someone that's a gastroenterologist who's also an</p> <p>9 expert in immunology -- immunology related to the</p> <p>10 GI system." And then I asked, "Why me?" And he</p> <p>11 said, "Because I was looking for someone in the</p> <p>12 Southeastern part of the country because that's</p> <p>13 where I'm based, and my impression is that you're</p> <p>14 the best expert in that part of the United</p> <p>15 States."</p> <p>16 Q. At the time you were contacted on</p> <p>17 this case, had you ever published anything</p> <p>18 regarding olmesartan?</p> <p>19 A. No.</p> <p>20 Q. At the time you were contacted in</p> <p>21 this case, had you ever published any articles</p> <p>22 regarding celiac disease?</p> <p>23 A. No.</p> <p>24 Q. At the time you were contacted in</p>	<p style="text-align: right;">Page 16</p> <p>1 you have not been involved either in a research</p> <p>2 or a clinical context with the evaluation or</p> <p>3 treatment of a patient with a gastrointestinal</p> <p>4 syndrome or presentation where olmesartan is</p> <p>5 considered to be a potential cause?</p> <p>6 A. That's correct.</p> <p>7 Q. Do you know whether or not</p> <p>8 physicians at Vanderbilt where you work have</p> <p>9 diagnosed any patients with what is described in</p> <p>10 the literature as olmesartan-associated</p> <p>11 enteropathy, olmesartan-induced enteropathy?</p> <p>12 A. So I'm a professor at Vanderbilt,</p> <p>13 but I -- and I have clinical privileges at</p> <p>14 Vanderbilt hospital, but I don't actually do any</p> <p>15 attending work there and don't see patients</p> <p>16 there. All of my clinical work is done at the</p> <p>17 adjacent Veterans Affairs hospital, and I've</p> <p>18 never heard of or seen any patient on olmesartan.</p> <p>19 So I'm not aware of anything.</p> <p>20 Q. Let's just flesh that out.</p> <p>21 You -- you work for Vanderbilt</p> <p>22 University Medical Center; correct?</p> <p>23 A. Correct, but I'm also a part-time</p> <p>24 government employee. I have partial salary</p>
<p style="text-align: right;">Page 15</p> <p>1 this case, had you ever been involved either in a</p> <p>2 research or a clinical capacity with a patient</p> <p>3 evaluation or treatment where olmesartan was a</p> <p>4 potential cause of a gastrointestinal syndrome?</p> <p>5 A. No.</p> <p>6 MR. CHRISTIAN: Objection. Form.</p> <p>7 THE WITNESS: Oh. No.</p> <p>8 BY MR. SLATER:</p> <p>9 Q. With regard to those three</p> <p>10 questions, are the answers the same right up</p> <p>11 until today?</p> <p>12 A. I don't understand your question.</p> <p>13 Q. You were contacted initially it</p> <p>14 looks like in the summer of 2016; right?</p> <p>15 A. Correct.</p> <p>16 Q. As of today, am I correct that</p> <p>17 you've never published any articles regarding</p> <p>18 olmesartan?</p> <p>19 A. That's correct.</p> <p>20 Q. Am I correct that as of today,</p> <p>21 you've never published any articles regarding</p> <p>22 celiac disease?</p> <p>23 A. Correct.</p> <p>24 Q. Am I correct that as of today,</p>	<p style="text-align: right;">Page 17</p> <p>1 support from the Department of Veterans Affairs.</p> <p>2 Q. Okay. Move to strike from "but"</p> <p>3 forward.</p> <p>4 I just want to talk about</p> <p>5 Vanderbilt for a couple minutes.</p> <p>6 A. Sure.</p> <p>7 Q. You're employed by Vanderbilt</p> <p>8 University Medical Center; correct?</p> <p>9 A. Yes.</p> <p>10 Q. Okay. Is your work at Vanderbilt</p> <p>11 limited to -- well, rephrase.</p> <p>12 At Vanderbilt, my understanding</p> <p>13 is that you have certain administrative duties in</p> <p>14 your department; correct?</p> <p>15 A. Correct.</p> <p>16 Q. You also do research --</p> <p>17 A. Correct.</p> <p>18 Q. -- correct?</p> <p>19 How much time do you spend on</p> <p>20 clinical treatment of patients at Vanderbilt on a</p> <p>21 monthly basis?</p> <p>22 A. At Vanderbilt? None.</p> <p>23 Q. Other than Vanderbilt, where do</p> <p>24 you work professionally?</p>

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<p style="text-align: right;">Page 18</p> <p>1 A. The Nashville VA Medical Center, 2 which is part of the Tennessee VA healthcare 3 system. 4 Q. How much time a month do you 5 spend working at Nashville VA? 6 A. So I would estimate that it's 7 about 10 hours per week. So that would be 40 to 8 50 hours a month on average amortized over the 9 course of the year. 10 Q. The 10 hours per week at the 11 Nashville VA, what are they spent doing? 12 A. So every Wednesday I do endoscopy 13 for about five hours where I'm sometimes doing 14 cases by myself. Other times I'm -- most of the 15 time I'm doing cases with our fellows, who are 16 young doctors who have completed residency and 17 are doing a three-year fellowship. And then four 18 weeks of the year I do inpatient consult 19 attending. 20 Q. When you say "inpatient 21 consultation," does that mean where a patient has 22 been admitted to the hospital and you'll be, as 23 part of the staff, called in for a consultation 24 if there's a gastrointestinal issue?</p>	<p style="text-align: right;">Page 20</p> <p>1 So there's -- there's a department of med -- 2 there's an internal medicine attending, but 3 there's lots of other attendings from surgery and 4 GI and nephrology, whatever that see the patient, 5 and we all feel that we're responsible for the 6 issues in front of us. 7 Q. Okay. In the last -- rephrase. 8 When is the last time you were 9 involved in the treatment of a patient who was 10 being treated for symptoms of celiac disease? 11 A. So you're saying the treatment. 12 We often are working up patients for celiac 13 disease, but we have a group practice where 14 there's a clinic that is staffed by two 15 attendings. I don't do that, and so if a patient 16 were diagnosed with celiac disease, they'd be 17 followed in that clinic and managed by the 18 fellows that are in training and a different 19 attending than me. 20 Q. When is the last time you were 21 involved in -- well, rephrase. 22 When is the last time you 23 diagnosed a patient with celiac disease? 24 A. I can't recall really because we</p>
<p style="text-align: right;">Page 19</p> <p>1 A. Yes. 2 Q. They're not your patients per se. 3 You're asked to consult on someone else's 4 patient; is that correct? 5 A. Well, that's an interesting 6 philosophical question. 7 Technically there's an attending 8 of record. However, I will say that our service 9 chief at the VA always preaches to us that when 10 their primary problem is a GI one, that we should 11 really try and take ownership of the patients and 12 make sure that everything is being done exactly 13 right. So sometimes our trainees will even write 14 orders on the patients. 15 Q. Okay. When you see a patient at 16 the Nashville VA as an inpatient, am I correct 17 you would not be listed as the attending 18 physician for that patient? 19 A. That's correct. However, let me 20 clarify. It's not like a private hospital where 21 in the old days when there would be a stamp for 22 the name of the patient and above it would be the 23 name of their one assigned attending. At the VA, 24 it's really a group practice for all patients.</p>	<p style="text-align: right;">Page 21</p> <p>1 take biopsies, and the fellows are the ones that 2 do the follow-up. So I would say probably 3 several times a month we're taking biopsies from 4 the duodenum to evaluate people with 5 iron-deficiency anemia to rule out celiac but, 6 frankly speaking, I don't check the follow-up of 7 those biopsies. So I -- that's somebody else's 8 job. So I actually can't answer that question. 9 Q. So you're involved in the process 10 whereby the biopsies are taken, but you're not 11 part of the follow-up to evaluate the result and 12 make a diagnosis and a -- and a recommendation to 13 the patient; correct? 14 A. Right, because, for example, we 15 have our service chief and our director of 16 endoscopy at the VA, and they're full time VA and 17 they're over there every day. I'm just there one 18 day a week. So it's not part of my 19 responsibilities. 20 Q. Have you spoken to any other 21 physicians in connection with your work in this 22 case? 23 A. So I did ask a couple of my 24 colleagues at the VA if they had ever seen a case</p>

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<p style="text-align: right;">Page 22</p> <p>1 of olmesartan-associated GI symptoms, and they --</p> <p>2 they were a couple of my colleagues at the VA and</p> <p>3 they both had never heard of the situation.</p> <p>4 Q. They hadn't -- they were not</p> <p>5 aware of the condition?</p> <p>6 A. Right.</p> <p>7 Q. They hadn't heard of the fact</p> <p>8 that it existed?</p> <p>9 A. That's correct.</p> <p>10 Q. And these are</p> <p>11 gastroenterologists?</p> <p>12 A. Yes.</p> <p>13 Q. Before you were contacted in this</p> <p>14 case, had you heard of olmesartan-associated</p> <p>15 enteropathy, this condition that's at issue in</p> <p>16 this litigation?</p> <p>17 A. No.</p> <p>18 Q. Is it fair to assume that you had</p> <p>19 not read any literature or articles about this</p> <p>20 condition, olmesartan-associated enteropathy,</p> <p>21 before you were contacted?</p> <p>22 A. That's correct.</p> <p>23 Q. You know Joseph Murray; correct?</p> <p>24 A. Yes.</p>	<p style="text-align: right;">Page 24</p> <p>1 many articles by looking at the title or starting</p> <p>2 to skim the abstract, and then if I don't feel</p> <p>3 like it's useful, I just move on.</p> <p>4 So there certainly were other</p> <p>5 things that I might have searched on which I</p> <p>6 can't give you specifics now, but I use PubMed</p> <p>7 every day, and I might have encountered other</p> <p>8 articles that I started to read the abstract and</p> <p>9 just felt that they were not important enough for</p> <p>10 me to download the whole article or read it or</p> <p>11 anything like that. So I can't give you any</p> <p>12 specifics.</p> <p>13 I would just say that I did</p> <p>14 peruse the general literature beyond my reliance</p> <p>15 list, but I very carefully selected the articles</p> <p>16 to comment on in my report based on the ones that</p> <p>17 I felt from my vantage point were the most</p> <p>18 important.</p> <p>19 Q. Am I correct that your</p> <p>20 understanding of the clinical diagnosis and</p> <p>21 clinical management of olmesartan-associated</p> <p>22 enteropathy comes entirely from what you've read</p> <p>23 in medical literature?</p> <p>24 A. Right.</p>
<p style="text-align: right;">Page 23</p> <p>1 Q. Essentially a world-renowned</p> <p>2 gastroenterologist in the field of celiac</p> <p>3 disease?</p> <p>4 A. I would say so.</p> <p>5 Q. In looking at your invoice,</p> <p>6 Exhibit 3?</p> <p>7 A. Yes.</p> <p>8 Q. It says "Review of medical</p> <p>9 literature." This is the third entry. "Review</p> <p>10 of medical literature in advance of December 10,</p> <p>11 2016 conference."</p> <p>12 Is that the first time you</p> <p>13 reviewed medical literature with regard to</p> <p>14 olmesartan-associated enteropathy?</p> <p>15 A. Yes.</p> <p>16 Q. Am I correct that your</p> <p>17 understanding of the clinical diagnosis and</p> <p>18 management of olmesartan-associated enteropathy,</p> <p>19 your knowledge of that is limited to what you've</p> <p>20 read in the literature that's listed in your</p> <p>21 report and reliance list?</p> <p>22 A. Yes. The only caveat I would say</p> <p>23 is that in my job, I often many, many times look</p> <p>24 for things on PubMed and will glance at many,</p>	<p style="text-align: right;">Page 25</p> <p>1 Q. And if I understand correctly,</p> <p>2 the sources you found to be most important and</p> <p>3 those that you're relying on are those you</p> <p>4 actually cited to in your report and listed on</p> <p>5 your reliance lists?</p> <p>6 A. That's correct.</p> <p>7 Q. You've seen some other literature</p> <p>8 from time to time since you were retained in this</p> <p>9 case, but none of it you felt was important</p> <p>10 enough to list; fair?</p> <p>11 A. That -- yes, that's fair.</p> <p>12 Q. Did you request any documents</p> <p>13 from the lawyers who hired you in this case?</p> <p>14 A. Could you be more specific?</p> <p>15 Q. I've looked at your reliance</p> <p>16 list. I see that you listed various articles;</p> <p>17 correct?</p> <p>18 A. Yes.</p> <p>19 Q. Was there anything that you felt</p> <p>20 you wanted to see that you asked the lawyers,</p> <p>21 could you provide this to me as part of my review</p> <p>22 of the case? Is there anything you asked them</p> <p>23 for?</p> <p>24 A. Well, the way it actually worked</p>

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<p style="text-align: right;">Page 26</p> <p>1 was initially I was provided a list of some 2 articles and then I found others on my own, but 3 once I needed to find more articles, I just 4 downloaded them myself. 5 Q. The list of articles you were 6 originally provided, do you have that list? 7 A. Yes. 8 Q. In looking -- let's -- let's do 9 this. Exhibit 4 we've marked. 10 It's my understanding that's your 11 report. It's the list of references, your 12 reliance list, and it's your curriculum vitae; 13 correct? 14 A. Let me just look and see what you 15 have here. 16 So the only thing that Exhibit 4 17 is, is just my CV. I don't see my -- my report 18 is not included in that. 19 Q. All right. Well, then we need to 20 re-mark this. There should have been -- we sent 21 down the expert report general causation. That 22 should be the first page of this. 23 A. No. 24 MR. SLATER: So I'm asking the</p>	<p style="text-align: right;">Page 28</p> <p>1 Q. Okay. And there's a list of 2 references and materials reviewed on page 19 of 3 your report? 4 A. Yes. 5 Q. Okay. Were any of the materials 6 listed on page 19 and 20 materials that you found 7 on your own as opposed to having been provided on 8 the original list from counsel? 9 A. Yes, there are. In terms of me 10 trying to find each one, it would take me a few 11 minutes, if that's what you would like me to do. 12 Q. I just wanted -- let me ask you 13 this. 14 Are you able to tell me real 15 quick if you just ran through the -- there's two 16 items listed 1 and 2 and then 1 through 24. 17 Do you know as you go through it 18 quickly which you found on your own? 19 A. So 1 and 2 were online resources, 20 UpToDate and Sleisinger, which I access through 21 the Vanderbilt library. So that wasn't on the 22 original list. I believe that reference 2 was 23 referred to in the 2012 paper. So I downloaded 24 that and looked at that, and then Cartee,</p>
<p style="text-align: right;">Page 27</p> <p>1 court reporter. Do you have that there? 2 It was sent down. 3 THE REPORTER: Yes. 4 MR. SLATER: All right. Let's 5 mark that as Exhibit 4 because that 6 should have attached to it the reliance 7 list, which is part of the report, 8 actually, and his CV. 9 (Exhibit 4 re-marked). 10 THE WITNESS: So this is 5 and 11 this is 4. So this is obsolete. 12 (Reviewing document). 13 THE WITNESS: Okay. So this is 14 the wrong version of my CV. This is the 15 one from January 27th. I provided an 16 updated one that was dated. 17 BY MR. SLATER: 18 Q. That's fine. I'm going to mark 19 the updated CV as a different exhibit. 20 A. Okay. 21 Q. So do we now have the report 22 marked as Exhibit 4 which had your CV that was up 23 to date as of the time the report was served? 24 A. Yes.</p>	<p style="text-align: right;">Page 29</p> <p>1 reference 3, was not in that original list. 2 Theophile was. Marthey was. Brown was not. I 3 found -- 4 Q. Tell me the ones that weren't. 5 You can just tell me the numbers of the ones that 6 weren't. 7 A. Okay. So the 1 and 2 above the 8 references and then 2 wasn't, 3 wasn't, 6 wasn't, 9 7 wasn't. 10 I'm not finding 8 in that 11 original list either. 12 I'm just checking these one by 13 one. 14 16 and 17 were not. 15 (Reviewing document). 16 Q. Any others? 17 A. I'm still -- okay. No. I'm down 18 to 22. Just give me a minute. 19 Okay. 22, 23 were not. That's 20 it. 21 Q. Okay. 22 A. Plus the in the -- 23 Q. And you were consulting a list 24 that counsel provided you?</p>

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<p style="text-align: right;">Page 30</p> <p>1 A. Uh-huh. Yes.</p> <p>2 MR. SLATER: Let's mark that as</p> <p>3 an exhibit, whatever we're up to. Let's</p> <p>4 just get that marked.</p> <p>5 THE REPORTER: Exhibit 6.</p> <p>6 (Document marked for</p> <p>7 identification purposes as Gutman</p> <p>8 Exhibit 6.)</p> <p>9 THE WITNESS: Then in the</p> <p>10 supplemental reliance list, items 1</p> <p>11 through 6 were all items that I found on</p> <p>12 my own that were not part of the list.</p> <p>13 BY MR. SLATER:</p> <p>14 Q. And the supplemental reliance</p> <p>15 list is what we marked as Exhibit 5; correct?</p> <p>16 A. Yes.</p> <p>17 Q. Okay. I will come back to that.</p> <p>18 Looking at page 19 of your</p> <p>19 report, UpToDate, what did you look at on</p> <p>20 UpToDate?</p> <p>21 A. I looked on celiac disease and I</p> <p>22 looked up acute diarrhea, chronic diarrhea.</p> <p>23 Those are the main things that I recall.</p> <p>24 Q. Did you look for the causes of</p>	<p style="text-align: right;">Page 32</p> <p>1 general overview of the workup of acute and</p> <p>2 chronic diarrhea. So that was the main reason I</p> <p>3 consulted it.</p> <p>4 Q. Do physicians in clinical</p> <p>5 practice routinely consult UpToDate for</p> <p>6 information about medications and side effects,</p> <p>7 that sort of thing?</p> <p>8 A. I, frankly, can't really say what</p> <p>9 other doctors do. I just know that on occasion I</p> <p>10 will. If I see a patient in the hospital and I</p> <p>11 see something that I feel like I need a refresher</p> <p>12 on, I'll just go to it because it's the fastest</p> <p>13 thing I can think of. I'll either do that or</p> <p>14 just run a PubMed first.</p> <p>15 Q. Do you consider -- do you</p> <p>16 consider UpToDate to be a reliable source of</p> <p>17 medical information?</p> <p>18 A. You know, with the caveat that</p> <p>19 it's written, there's no peer review. It's just</p> <p>20 -- it's somewhat reliable, but it's not as</p> <p>21 reliable as a peer-reviewed randomized controlled</p> <p>22 trial. So --</p> <p>23 Q. Have you relied on UpToDate in</p> <p>24 the course of evaluating or treating patients you</p>
<p style="text-align: right;">Page 31</p> <p>1 villous atrophy or sprue enteropathy on UpToDate?</p> <p>2 A. I don't remember.</p> <p>3 Q. Did you see anything on UpToDate</p> <p>4 indicating that olmesartan causes villous atrophy</p> <p>5 or enteropathy, anything of that nature?</p> <p>6 A. No.</p> <p>7 Q. I didn't hear your answer. Did</p> <p>8 you say no?</p> <p>9 A. No.</p> <p>10 Q. You went to UpToDate because --</p> <p>11 well, rephrase.</p> <p>12 Why did you consult UpToDate?</p> <p>13 A. It's something that I'm very used</p> <p>14 to using. In the VA, whenever you're seeing a</p> <p>15 patient, you can actually -- within the</p> <p>16 electronic medical record system, you can just</p> <p>17 use a pulldown to -- to add as a tool, and it</p> <p>18 brings up a direct link to UpToDate. So I don't</p> <p>19 use it often, but I use it occasionally and I</p> <p>20 like it, and it's a good way to read up on --</p> <p>21 it's kind of a living document.</p> <p>22 It's something that experts</p> <p>23 periodically update their sections, and I just</p> <p>24 thought it would be a good way to get a nice</p>	<p style="text-align: right;">Page 33</p> <p>1 were involved with?</p> <p>2 A. In my life? Sure.</p> <p>3 Can I restate that? I don't know</p> <p>4 that I would use the word "rely." I rely on my</p> <p>5 clinical judgment. I may consult it to see what</p> <p>6 people are writing about current testing for</p> <p>7 what's the latest thinking about all the</p> <p>8 serologies you should consider for celiac disease</p> <p>9 or anything that might have come along, but,</p> <p>10 again, it's not a peer-reviewed source of</p> <p>11 information.</p> <p>12 Q. In your treatment or evaluation</p> <p>13 of patients, are there times where you will look</p> <p>14 up information on UpToDate and incorporate that</p> <p>15 information into your decision-making?</p> <p>16 A. Very rarely.</p> <p>17 Q. Why bother looking at them? I</p> <p>18 mean, I'm not sure. You said you look at it and</p> <p>19 now it sounds like --</p> <p>20 A. It's a quick --</p> <p>21 Q. -- you're telling me it's like</p> <p>22 something that you wouldn't even, it's like a</p> <p>23 comic book. I can't get -- I can't get a sense</p> <p>24 from you what it is. I mean, so let's try to pin</p>

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<p style="text-align: right;">Page 34</p> <p>1 it down. So let me ask you this question.</p> <p>2 You look at UpToDate from time to</p> <p>3 time in your own medical practice; correct?</p> <p>4 A. I'd say maybe two times a year.</p> <p>5 Q. You looked up -- rephrase.</p> <p>6 You consulted UpToDate as part of</p> <p>7 your educational process for yourself as to be an</p> <p>8 expert in this case; right?</p> <p>9 A. Yes.</p> <p>10 Q. Small intestinal villous atrophy</p> <p>11 other than celiac disease on UpToDate?</p> <p>12 A. I don't remember looking at that.</p> <p>13 Q. You certainly didn't mention that</p> <p>14 anywhere in your report; correct?</p> <p>15 A. I don't recall. Is there</p> <p>16 something in my report about that?</p> <p>17 Q. I'm saying, you didn't say</p> <p>18 anything about that in your report; right?</p> <p>19 A. Not that I can recall.</p> <p>20 Q. You mentioned UpToDate other than</p> <p>21 on page 19 where you list it as a material</p> <p>22 reviewed; is that correct?</p> <p>23 A. Yes.</p> <p>24 I can point out to you the</p>	<p style="text-align: right;">Page 36</p> <p>1 there "diarrhea evaluation" or something like</p> <p>2 that and found what they said.</p> <p>3 Q. So in reviewing UpToDate, you</p> <p>4 didn't find the fact that it lists causes of</p> <p>5 small intestinal villous atrophy other than</p> <p>6 celiac disease, and one of those listed is</p> <p>7 medications, for example, olmesartan? You didn't</p> <p>8 see that when you went on UpToDate, did you?</p> <p>9 MR. CHRISTIAN: Objection. Form.</p> <p>10 THE WITNESS: I honestly can't</p> <p>11 recall because I wrote this report over a</p> <p>12 month ago, and I don't remember reading</p> <p>13 that.</p> <p>14 BY MR. SLATER:</p> <p>15 Q. Anywhere; correct?</p> <p>16 A. To my recollection.</p> <p>17 Q. I'm saying, that's not referenced</p> <p>18 anywhere in your report; right?</p> <p>19 A. No.</p> <p>20 Q. On page 19, you list Sleisenger</p> <p>21 and Fordtran's "Gastrointestinal and Liver</p> <p>22 Disease." What is that?</p> <p>23 A. So that's a textbook that when I</p> <p>24 was in my training was sort of considered the</p>
<p style="text-align: right;">Page 35</p> <p>1 section where I utilized it primarily was pages</p> <p>2 13 --</p> <p>3 Q. Fine. Where is that?</p> <p>4 A. Pages 13 to 14.</p> <p>5 Sorry. It's actually just</p> <p>6 through the second paragraph on page 14.</p> <p>7 Q. The information on page 13</p> <p>8 through the second paragraph of page 14, was that</p> <p>9 all taken from UpToDate?</p> <p>10 A. I mean, I used UpToDate as a way</p> <p>11 for me to organize my thoughts, but some of what</p> <p>12 I wrote were -- what I wrote was just my own</p> <p>13 impression.</p> <p>14 Q. Try to do a thorough review of</p> <p>15 UpToDate to find relevant information relevant to</p> <p>16 this case and to your opinions?</p> <p>17 A. I didn't hear the beginning of</p> <p>18 what you said.</p> <p>19 Q. I say, did you attempt to be</p> <p>20 thorough in finding relevant information, meaning</p> <p>21 relevant to the opinions you were going to give</p> <p>22 in this case?</p> <p>23 A. I don't think I would say</p> <p>24 "thorough," no. I would say that I typed in</p>	<p style="text-align: right;">Page 37</p> <p>1 bible of gastroenterology, and so through the</p> <p>2 Vanderbilt online library I accessed that and</p> <p>3 skimmed through the chapter by Ciam Kelly about</p> <p>4 celiac disease.</p> <p>5 Q. Do you know what issue date that</p> <p>6 volume was or, you know, what that --</p> <p>7 A. So I believe it's --</p> <p>8 Q. -- location date was?</p> <p>9 MR. CHRISTIAN: Wait. Let him</p> <p>10 completely finish with his question.</p> <p>11 THE WITNESS: I'm sorry.</p> <p>12 So I know this is going to sound</p> <p>13 like a long-winded answer, but at the</p> <p>14 time that I was working on this, you</p> <p>15 could access Sleisenger through the</p> <p>16 Vanderbilt library and something has</p> <p>17 happened with their license for that</p> <p>18 because I tried to access it again a few</p> <p>19 weeks ago, and I couldn't find it at all.</p> <p>20 And then yesterday I was trying</p> <p>21 to show Randy what it was, and it came up</p> <p>22 and I clicked on it and it said, "This is</p> <p>23 no longer available at Vanderbilt." So</p> <p>24 I'm pretty certain it was the 2016</p>

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<p style="text-align: right;">Page 38</p> <p>1 edition, but I don't have a way of 2 verifying that and I can't access it 3 anymore. And the book costs like a 4 thousand dollars, so I'm certainly not 5 going to buy it. 6 BY MR. SLATER: 7 Q. Did you look to see if there was 8 any discussion of olmesartan anywhere in the 9 book? 10 A. So I only looked at the chapter 11 by Kelly, who's somebody from the Beth Israel in 12 Boston who I know, and there was no mention of 13 olmesartan in his chapter, but there was a very 14 nice algorithm of how to work up patients with 15 possible celiac disease. 16 Q. So you looked at a chapter in the 17 Sleisenger and Fordtran book regarding celiac 18 written by Dr. Kelly? 19 A. Yes. 20 Q. Did you look to see if there was 21 any discussion of olmesartan or whether that drug 22 was even mentioned anywhere in the book? 23 A. No. It's kind of cumbersome 24 trying to figure out how to use these online</p>	<p style="text-align: right;">Page 40</p> <p>1 MR. CHRISTIAN: Adam, we missed 2 the first couple of words of your 3 question. 4 BY MR. SLATER: 5 Q. As to what, if any, findings the 6 company has made with regard to whether 7 olmesartan causes what has been described in the 8 literature as olmesartan-associated enteropathy? 9 A. I -- 10 MR. CHRISTIAN: Objection. Form. 11 THE WITNESS: Shall I answer? 12 MR. CHRISTIAN: Yeah. 13 THE WITNESS: I have no 14 information whatsoever about anything at 15 the company. 16 BY MR. SLATER: 17 Q. Were you curious as to whether 18 Daiichi was studying the question that you were 19 asked to give an opinion on? 20 MR. CHRISTIAN: Objection. Form. 21 THE WITNESS: I don't know much 22 about the business world or 23 pharmaceutical industry. I am an expert 24 in my own world but -- so, therefore, I</p>
<p style="text-align: right;">Page 39</p> <p>1 resources. It's -- it's kind of hard to explain, 2 but you basically -- you sort of see this Table 3 of Contents, and then I just clicked on the 4 chapter for celiac disease. It's not really very 5 easily searchable. So that was all that I looked 6 at. 7 Q. Okay. Move to strike after "no." 8 Did any -- rephrase. 9 Were you provided any internal 10 Daiichi documents, meaning documents from the 11 company? 12 A. No. 13 Q. Were you provided any depositions 14 of any Daiichi witnesses? 15 A. No. 16 Q. Do you have any understanding of 17 the inner workings of Daiichi, for example, who 18 is responsible to evaluate potential adverse drug 19 reactions from their medications? 20 A. No. 21 Q. As to what evaluation Daiichi has 22 done as to whether there is a causal relationship 23 between olmesartan and olmesartan-associated 24 enteropathy?</p>	<p style="text-align: right;">Page 41</p> <p>1 assume that it's very complicated and 2 wouldn't really try and go there. 3 BY MR. SLATER: 4 Q. It is fair to say that you formed 5 certain opinions in this case. They were based 6 on your own education and knowledge, what you 7 bring to the case. That was one thing you 8 brought to it; right? 9 A. Yes. 10 Q. Did you say yes? 11 A. Yes. 12 Q. Okay. We sometimes fade out each 13 way. So I'm not trying to be rude. It's just 14 sometimes I can't tell if you answered. 15 The other thing that you 16 considered in forming your opinions was medical 17 literature that you read; correct? 18 A. Yes. 19 Q. You mentioned these other two 20 things that we talked about a moment ago. 21 You looked on UpToDate and you 22 looked at the Sleisenger text, the chapter on 23 celiac disease; correct? 24 A. Correct.</p>

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<p style="text-align: right;">Page 42</p> <p>1 Q. Those -- those sources of</p> <p>2 information were what you relied on in forming</p> <p>3 your opinions in this case; correct?</p> <p>4 A. Yes.</p> <p>5 Q. Okay. You did not rely to any</p> <p>6 extent on clinical experience with the evaluation</p> <p>7 or diagnosis of a potential olmesartan-related</p> <p>8 gastrointestinal illness because you have no such</p> <p>9 experience; correct?</p> <p>10 A. Correct.</p> <p>11 Q. Tell me if I'm correct if I boil</p> <p>12 down what your opinion is in this case.</p> <p>13 If I understand correctly, you've</p> <p>14 essentially done a review of the literature that</p> <p>15 you've listed in your report and your reliance</p> <p>16 lists, and essentially after a review of the</p> <p>17 literature, giving your opinion about the</p> <p>18 strength of the literature in terms of the</p> <p>19 strength of the studies and whether from your</p> <p>20 review of the literature whether you think there</p> <p>21 is an association or a causal relationship shown</p> <p>22 by those studies described in the medical</p> <p>23 literature.</p> <p>24 Is that a fair overview of what</p>	<p style="text-align: right;">Page 44</p> <p>1 Q. With regard to the question of</p> <p>2 whether or not a drug causes an adverse drug</p> <p>3 reaction, if you're trying to answer that</p> <p>4 question, application of the Bradford Hill</p> <p>5 criteria is an accepted scientific methodology;</p> <p>6 correct?</p> <p>7 A. I don't know that I want to just</p> <p>8 say it's accepted by everyone. It's a type of</p> <p>9 nomenclature that is -- I was asked to address,</p> <p>10 whether I felt that the articles -- how they fit</p> <p>11 in that context. So I, you know, I'm not able to</p> <p>12 say whether every epidemiologist feels that the</p> <p>13 Bradford Hill criteria needs to be applied for</p> <p>14 every situation.</p> <p>15 Q. Your expertise is</p> <p>16 gastroenterology and, more specifically,</p> <p>17 immunology in the context of gastroenterology.</p> <p>18 Is that a fair overview of your</p> <p>19 expertise?</p> <p>20 A. I think that's a little bit</p> <p>21 limiting. I hold three professorships at</p> <p>22 Vanderbilt. Department of -- professor of</p> <p>23 medicine. I'm also a professor of cancer biology</p> <p>24 because a lot of my research relates to the</p>
<p style="text-align: right;">Page 43</p> <p>1 your opinion is?</p> <p>2 A. Yes.</p> <p>3 Q. One of the sources -- rephrase.</p> <p>4 One of the criteria you</p> <p>5 referenced in your report is the Bradford Hill</p> <p>6 criteria; correct?</p> <p>7 A. Yes.</p> <p>8 Q. And the utilization of the</p> <p>9 Bradford Hill criteria is an accepted scientific</p> <p>10 methodology to assess whether a drug is causing</p> <p>11 an adverse drug reaction; correct?</p> <p>12 A. I think it's more general than</p> <p>13 that. I don't think it's specific to whether a</p> <p>14 drug causes an adverse reaction. It's a way of</p> <p>15 evaluating.</p> <p>16 Q. I understand. You understand in</p> <p>17 this case the question is whether or not</p> <p>18 olmesartan causes, whatever you want to call it.</p> <p>19 Olmesartan-associated enteropathy we'll call it</p> <p>20 for the purposes of this case, okay?</p> <p>21 A. Okay.</p> <p>22 Q. You're asked to answer in this</p> <p>23 report; right?</p> <p>24 A. Yes.</p>	<p style="text-align: right;">Page 45</p> <p>1 process of carcinogenesis. And then I held a</p> <p>2 professorship in what's called pathology,</p> <p>3 microbiology, and immunology. So my expertise</p> <p>4 spans those areas.</p> <p>5 Also, I'm the principal</p> <p>6 investigator on multiple grants and I'm the PI,</p> <p>7 as I enumerated in my report, of two very large</p> <p>8 studies that have a large clinical translational</p> <p>9 component that deals with the etiology and</p> <p>10 prevention of cancer. So I have expertise in</p> <p>11 evaluating epidemiologic factors in terms of</p> <p>12 disease prevention.</p> <p>13 Q. The studies that you have</p> <p>14 performed and are performing, none of them relate</p> <p>15 to olmesartan; correct?</p> <p>16 A. Correct.</p> <p>17 Q. The studies you've performed and</p> <p>18 are performing, none of them relate to celiac</p> <p>19 disease; correct?</p> <p>20 A. Correct.</p> <p>21 Q. You're not an epidemiologist;</p> <p>22 correct?</p> <p>23 A. Well, as I've said, I do not have</p> <p>24 a Ph.D. or a master's in Epi, but as the PI of</p>

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<p style="text-align: right;">Page 46</p> <p>1 two very large grants that about half of the 2 grants are epidemiologic in basis, I have a lot 3 of practical experience. 4 I've also mentored four trainees 5 that have gone through our master's program in 6 clinical investigation and served on the 7 admissions committee for that program for five 8 years. 9 So at Vanderbilt, I am considered 10 someone that has a lot of expertise about the 11 application of bench research to clinical 12 research. 13 Q. Do you know whether or not 14 Daiichi employs physicians who from time to time 15 evaluate adverse event reports regarding 16 olmesartan to determine whether there's a 17 probable or definite causal relationship? 18 A. I have no information about that. 19 So I would say I don't know. 20 Q. If there are physicians employed 21 by Daiichi who have reviewed adverse event 22 reports regarding olmesartan and gastrointestinal 23 syndromes reported with those patients and found 24 in some cases a probable or definite causal</p>	<p style="text-align: right;">Page 48</p> <p>1 Read a couple references that I listed there, and 2 that's how I knew what the Bradford Hill criteria 3 were. And I looked at things like level of 4 evidence and reviewed that, and I used all that 5 as a framework for writing my report. 6 But when I initially read all the 7 papers, it was just to look at them and get a 8 feel. Then I later applied that criteria. So it 9 was sort of a two-step process. 10 Q. Did you know what the Bradford 11 Hill criteria was before you were asked by 12 counsel to apply it? 13 A. No. 14 Q. So the decision to apply that 15 criteria was not part of your methodology. It 16 was what counsel asked you to do; correct? 17 MR. CHRISTIAN: Objection. Form. 18 THE WITNESS: So it turned out 19 that when I kind of looked at it, it's 20 sort of what we all do but, you know, 21 it's more of a legal standard in a sense 22 that it's from a very old reference from 23 the 1960s, and I don't know if it's even 24 part of the curriculum in the Master of</p>
<p style="text-align: right;">Page 47</p> <p>1 relationship, would you want to see those? 2 MR. CHRISTIAN: Objection. 3 BY MR. SLATER: 4 Q. Would you be interested to see 5 that? 6 MR. CHRISTIAN: Objection. Form. 7 THE WITNESS: I don't know what 8 those reports would look like. So I 9 don't know if they would be useful to me. 10 BY MR. SLATER: 11 Q. Did -- rephrase. 12 I think you said earlier that the 13 attorneys who retained you asked you to evaluate 14 the studies you were looking at, the literature 15 you were looking at under the Bradford Hill 16 criteria. 17 Did I understand that correctly? 18 A. After I looked at all the papers 19 and thought it through, and then in one of the 20 phone consultations it was indicated to me that 21 as I generate my report, I need to make reference 22 to the Bradford Hill criteria. 23 So then on my own, I looked up 24 the Bradford Hill criteria and read up on it.</p>	<p style="text-align: right;">Page 49</p> <p>1 Public Health or the Master of Clinical 2 Investigation programs that I'm familiar 3 with at Vanderbilt. 4 BY MR. SLATER: 5 Q. Is this report that you wrote in 6 this case the first time you have applied the 7 Bradford Hill criteria to an evaluation of a 8 question? 9 A. So what I would say is, 10 technically, yes. But if I could continue? 11 A lot of the concepts that are in 12 there are certainly things that as I fleshed out 13 what I thought that they meant, they are things 14 that I've always done in my career anyway. 15 Q. Move to strike after "yes." 16 You mentioned in your report the 17 Oxford Centre for Evidence-Based Medicine, some 18 criteria they utilize to evaluate the strength of 19 certain studies; correct? 20 A. Yes. 21 Q. Was that a criteria you were 22 familiar with before this case? 23 A. So not necessarily the exact 24 table that's on my page 2. However, every one of</p>

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<p style="text-align: right;">Page 50</p> <p>1 these features and the idea of grading levels of 2 evidence as a general concept is something that 3 I'm extremely familiar with, and that in our 4 conferences we'll always talk about whether 5 there's a meta-analysis that's been done and how 6 good that meta-analysis is and what kind of 7 randomized controlled trials and to remember that 8 RCTs are the most important thing compared to 9 retrospective studies.</p> <p>10 And this is a concept that -- I 11 took an epidemiology course when I was in medical 12 school at Harvard and it was taught by the 13 director of the Framingham Heart Study. So I -- 14 and I wrote an epidemiology honors thesis in 15 college. So I've been familiar with these 16 concepts going back for 35 years.</p> <p>17 Q. Okay. Move to strike.</p> <p>18 Before you were asked to work on 19 this report, had you ever read the Oxford Centre 20 for Evidence-Based Medicine levels of evidence? 21 Had you ever looked at that specific standard?</p> <p>22 A. No.</p> <p>23 Q. Was that standard given to you by 24 counsel?</p>	<p style="text-align: right;">Page 52</p> <p>1 standard to every study because in some studies 2 it's a little bit difficult to classify exactly 3 what type of study it is, particularly if it's a 4 small study, but I felt that I needed to look at 5 what some of the standards were. And I -- and I 6 found these things by Google and PubMed 7 searching.</p> <p>8 Q. Would you agree with me that a 9 drug can cause a side effect, even if there's no 10 randomized controlled trial that actually has 11 been utilized to show that causal relationship?</p> <p>12 A. So what I would say is that 13 practice patterns evolve as doctors use their own 14 practical experience, and they make decisions 15 about whether they think a medication might be 16 associated with particular side effects, and then 17 they have to decide whether they want to use that 18 medicine. But that may not represent Level I or 19 Level II evidence by any stretch.</p> <p>20 Q. A drug can cause an adverse drug 21 reaction, even if there's never been an RCT that 22 studied that question; correct?</p> <p>23 A. Yes.</p> <p>24 Q. A drug can cause an adverse drug</p>
<p style="text-align: right;">Page 51</p> <p>1 A. No.</p> <p>2 Q. Did counsel ask you to look at 3 that standard?</p> <p>4 A. No.</p> <p>5 Q. No?</p> <p>6 A. No.</p> <p>7 Q. Okay. Did you find the -- 8 rephrase.</p> <p>9 You reference in your report 10 the -- it's right on the first page, actually, 11 toward the bottom of the first page. The -- you 12 say -- let me ask a new question.</p> <p>13 On the first page of your report, 14 you say:</p> <p>15 "For this analysis, I will apply 16 standards of the Oxford Centre for Evidence-Based 17 Medicine," and then you have a citation that goes 18 through and talks about March 2009, etc.</p> <p>19 Do you see that?</p> <p>20 A. Yes.</p> <p>21 Q. Is that the standard you applied 22 in forming your opinions?</p> <p>23 A. Overall, I would say yes. I 24 mean, it's impossible to constantly apply that</p>	<p style="text-align: right;">Page 53</p> <p>1 reaction, even if the only published literature 2 on that subject is case reports. That can occur; 3 correct?</p> <p>4 A. Well, you're saying "can." So I 5 suppose that we know that there can be 6 idiosyncratic reactions to -- to essentially any 7 medication.</p> <p>8 Q. Let me ask you this. 9 You agree that NSAIDs can cause 10 gastrointestinal inflammation; correct?</p> <p>11 A. Yes.</p> <p>12 Q. NSAIDs cause gastrointestinal 13 inflammation, even before there were any studies 14 on that subject. The fact that the drug caused 15 that reaction was real, regardless of what 16 studies had been done on the question; right?</p> <p>17 MR. CHRISTIAN: Objection. Form.</p> <p>18 THE WITNESS: Well, I think you 19 need to be very careful with that because 20 there's probably on the order of more 21 than a hundred different types of 22 nonsteroidals and anti-inflammatories 23 that have been in the market over the 24 last 30 years, since I graduated from</p>

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<p style="text-align: right;">Page 54</p> <p>1 medical school, 31 years, and so it's a 2 well-known association. 3 It's very hard to be specific 4 about any particular one, however. 5 BY MR. SLATER: 6 Q. Okay. Did you actually go and 7 find the website for the Oxford Centre for 8 Evidence-Based Medicine on your own, or did 9 counsel tell you where to find that and direct 10 you to it? 11 A. I found it. 12 Q. And the standard you applied is 13 the one that is cited on page 1 of your report 14 and then listed on page 2; correct? 15 A. To the best of my ability, but as 16 I said with some of the studies, you may notice 17 in my report I said this is -- has some features 18 of Level II but also has some features of Level 19 IV, and so with some of the studies, I found it 20 was a bit difficult to pigeonhole. In other 21 words, they might be a case-control study but 22 have a very small N. 23 Q. All I'm asking is: The criteria 24 you applied from the Oxford Centre for</p>	<p style="text-align: right;">Page 56</p> <p>1 Q. Look at number 7 if you could. 2 A. That's within Exhibit 2? 3 Q. Yes. 4 That asks for any -- copies of 5 any documents, including protocols or information 6 about medications side effects from any hospital 7 or academic institution where you have worked, 8 had an appointment or had privilege which set 9 forth information related to the diagnosis or 10 treatment of any olmesartan/Benicar related 11 medications or medical conditions or side 12 effects. 13 A. Yes. 14 Q. Did you produce anything in 15 response to that request? 16 A. No. 17 MR. SLATER: Laura, could you -- 18 let's mark document 24, which is from the 19 Vanderbilt University website, please. 20 MS. PITTNER: Sure. 21 MR. SLATER: We'll mark that as 22 the next exhibit number. 23 THE REPORTER: Exhibit 7. 24 (Document marked for</p>
<p style="text-align: right;">Page 55</p> <p>1 Evidence-Based Medicine, the website and the 2 specific standard March 2009 and then the 3 Table 1, that's what you applied; correct? 4 A. Yeah. 5 MR. CHRISTIAN: Object to form. 6 THE WITNESS: Essentially, yes. 7 BY MR. SLATER: 8 Q. Let's just go back to one thing 9 before we go back into the substance. 10 If you could look at Exhibit 2, 11 again, please. The response to our deposition 12 notice. 13 A. Yes. 14 Q. We already established that you 15 produced the invoices that we marked as 16 Exhibit 3, which also have your worksheet for 17 February, which hasn't been billed to counsel 18 yet; right? 19 A. Correct. 20 Q. Are there any other documents 21 that you have produced or that you have in your 22 possession that are responsive to any of these 23 requests? 24 A. No.</p>	<p style="text-align: right;">Page 57</p> <p>1 identification purposes as Gutman 2 Exhibit 7.) 3 BY MR. SLATER: 4 Q. Doctor, Exhibit 7 is something 5 that we printed off of the Vanderbilt website on 6 February 15th, 10 days ago. Do you see that? 7 A. Yes. 8 Q. You work for Vanderbilt 9 University; correct? 10 A. Yes. 11 Q. And you see that the title of 12 this page, it looks like it's the Human Research 13 Protection Program supporting the work of the 14 IRB. 15 That would be the Institutional 16 Review Board; correct? 17 A. Yes. 18 Q. And providing HRPP oversight. 19 What is HRPP? 20 A. It's defined at the top here as 21 Human Research Protection Program. 22 Q. Do you know what the Human 23 Research Protection Program at Vanderbilt 24 University is?</p>

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<p style="text-align: right;">Page 58</p> <p>1 A. I don't know everything that it 2 encompasses, but I know that it is the oversight 3 for the IRB-associated research studies. 4 Q. And if you go down and look at 5 the title of this specific page within this 6 website, it says: 7 "FDA MedWatch - Olmesartan 8 Medoxomil: Drug Safety Communication - Label 9 Changes to Include Intestinal Problems 10 (Sprue-Like Enteropathy)." 11 Do you see that? 12 A. I see it. 13 Q. It actually says the audience is 14 health professionals, cardiology, and patients; 15 right? 16 A. Yes. 17 Q. And then the issue is listed, and 18 I'm just going to read the first part: 19 "FDA is warning that the blood 20 pressure drug Olmesartan Medoxomil (marketed as 21 Benicar, Benicar HCT, Azor, Tribenzor, and 22 generics) can cause intestinal problems known as 23 sprue-like enteropathy," and then there's a list 24 of symptoms.</p>	<p style="text-align: right;">Page 60</p> <p>1 that language? 2 MR. CHRISTIAN: One second. I 3 think he was still talking when you 4 started your next question, Adam. 5 Did you finish? 6 THE WITNESS: No. 7 BY MR. SLATER: 8 Q. I'm sorry. I didn't mean to. 9 A. I didn't finish. 10 Q. Was I? 11 A. What I was going to say was that, 12 it's my understanding that the FDA has issued a 13 warning in 2013 that clinicians should be aware 14 of this possible association. They've never said 15 that it can cause it. 16 Q. Okay. Now, looking at the 17 language that was posted on Vanderbilt 18 University's website, it says: 19 "The FDA is warning that the 20 blood pressure drug Olmesartan Medoxomil can 21 cause intestinal problems known as sprue-like 22 enteropathy." 23 My question is: Is this the 24 first time you're seeing anything in writing</p>
<p style="text-align: right;">Page 59</p> <p>1 Do you see that? 2 A. Yes. 3 Q. Are you aware that the position 4 of the FDA is that olmesartan can cause 5 sprue-like enteropathy? 6 MR. CHRISTIAN: Objection. Form. 7 THE WITNESS: That's -- to my 8 understanding, that's not their position. 9 Their position is that it -- it 10 may cause -- it has the potential to 11 cause problems. So that if you as a 12 clinician think that you have a patient 13 that's on it and you believe that there 14 could be some association, you should 15 consider stopping the medication. 16 It does not -- 17 BY MR. SLATER: 18 Q. Is this the first time you've 19 seen something documenting that the FDA has 20 warned that olmesartan can cause intestinal 21 problems known as sprue-like enteropathy? 22 MR. CHRISTIAN: Adam. 23 BY MR. SLATER: 24 Q. Is this your first time seeing</p>	<p style="text-align: right;">Page 61</p> <p>1 indicating that the FDA believes that olmesartan 2 can cause sprue-like enteropathy? 3 MR. CHRISTIAN: Objection. Form. 4 THE WITNESS: This is not the 5 first time that I have been made aware 6 that the FDA issued a change to the 7 product insert in 2013. 8 BY MR. SLATER: 9 Q. My question -- move to strike. 10 My question was: Is this the 11 first time you're seeing language indicating that 12 the FDA believes that olmesartan can cause 13 sprue-like enteropathy? Is this the first time 14 you're seeing that language? 15 MR. CHRISTIAN: Objection. Form. 16 THE WITNESS: Frankly, I can't 17 recall the exact language in the FDA 18 product insert alteration because I 19 haven't looked at that in over a month. 20 BY MR. SLATER: 21 Q. One of the things you wanted to 22 do in forming an opinion in this case was to 23 consider all relevant evidence on either side of 24 the question to give a valid opinion; right?</p>

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<p>1 A. Correct.</p> <p>2 Q. And, for example, if there was</p> <p>3 important evidence -- rephrase.</p> <p>4 If there was documentary evidence</p> <p>5 or deposition testimony from people at Daiichi</p> <p>6 who are responsible for the safety of the</p> <p>7 olmesartan drugs, that could be something that</p> <p>8 would be important to you in rendering an</p> <p>9 opinion. You haven't seen any of it, but you</p> <p>10 would agree in general that could be important if</p> <p>11 you were shown that; right?</p> <p>12 MR. CHRISTIAN: Objection. Form.</p> <p>13 THE WITNESS: I don't agree</p> <p>14 because I was asked to evaluate the</p> <p>15 medical and scientific literature and</p> <p>16 that's just opinion and uncontrolled</p> <p>17 information, as is these -- this</p> <p>18 reference on the Vanderbilt website.</p> <p>19 This is just a pro forma</p> <p>20 regurgitation of something that was</p> <p>21 written by the FDA. It's not scientific</p> <p>22 evidence.</p> <p>23 BY MR. SLATER:</p> <p>24 Q. To understand, you just said you</p>	<p>1 around with --</p> <p>2 Q. This recommendation is specific</p> <p>3 to olmesartan; correct?</p> <p>4 A. Shall I go back and finish my</p> <p>5 previous statement?</p> <p>6 MR. CHRISTIAN: Yes. Yes.</p> <p>7 THE WITNESS: What I was saying</p> <p>8 before was that, no patient should be</p> <p>9 walking around with symptoms of this</p> <p>10 nature as described here without telling</p> <p>11 a healthcare professional, and then the</p> <p>12 healthcare professional would need to do</p> <p>13 an appropriate workup and an assessment</p> <p>14 of all medications they were on.</p> <p>15 And there's many other</p> <p>16 medications, hundreds that are linked to</p> <p>17 development of diarrhea. So there should</p> <p>18 be vigilance about looking for any</p> <p>19 medication.</p> <p>20 BY MR. SLATER:</p> <p>21 Q. Move to strike.</p> <p>22 This recommendation is to tell a</p> <p>23 patient who is prescribed olmesartan, specific to</p> <p>24 olmesartan, if you have this clinical picture,</p>
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<p>1 were only asked to evaluate the scientific</p> <p>2 literature and to form an opinion based on the</p> <p>3 literature; right?</p> <p>4 A. Yes.</p> <p>5 Q. Go to the second page of this</p> <p>6 document. There's a recommendation. The</p> <p>7 recommendation says:</p> <p>8 "Health care professionals should</p> <p>9 tell patients to contact them if they develop</p> <p>10 severe, chronic diarrhea with substantial weight</p> <p>11 loss while taking an olmesartan-containing</p> <p>12 product, even if it takes months to years for</p> <p>13 symptoms to develop."</p> <p>14 I want to stop there.</p> <p>15 You see what I just read?</p> <p>16 A. Yes.</p> <p>17 Q. That is a reasonable</p> <p>18 recommendation to physicians; correct?</p> <p>19 A. I think it's always -- any</p> <p>20 patient that would have severe, chronic diarrhea</p> <p>21 with weight loss needs to tell their doctor about</p> <p>22 it. There's nothing specific about that in</p> <p>23 olmesartan.</p> <p>24 So no one should be walking</p>	<p>1 severe, chronic diarrhea with substantial weight</p> <p>2 loss while taking an olmesartan-containing</p> <p>3 product, even if it takes months to years for</p> <p>4 symptoms to develop, you should come back to me</p> <p>5 as the physician and tell me this is happening</p> <p>6 while you're on olmesartan.</p> <p>7 That's the recommendation;</p> <p>8 correct?</p> <p>9 A. It's what's written, but what I</p> <p>10 would like to explain is, I don't know who wrote</p> <p>11 this. I think this is just the FDA's</p> <p>12 recommendation that's pasted onto the Vanderbilt</p> <p>13 website.</p> <p>14 I am not aware that the P&T</p> <p>15 Committee at Vanderbilt reviewed this and wrote</p> <p>16 this. I'm not aware that any gastroenterologists</p> <p>17 were consulted. I really don't think that this</p> <p>18 is a website that is designed to provide strong</p> <p>19 clinical recommendations. This is a website</p> <p>20 that's sort of a repository of information about</p> <p>21 clinical research.</p> <p>22 Q. Move to strike from "but"</p> <p>23 forward.</p> <p>24 The second sentence says:</p>

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<p style="text-align: right;">Page 66</p> <p>1 Patients should contact their</p> <p>2 health care professional right away if they take</p> <p>3 an olmesartan-containing product and experience</p> <p>4 severe diarrhea, diarrhea that does not go away,</p> <p>5 or significant weight loss."</p> <p>6 Do you see what I just read?</p> <p>7 A. Yes. Yes.</p> <p>8 Q. It is reasonable for a physician</p> <p>9 to tell a patient who is prescribed an</p> <p>10 olmesartan-containing drug, if you develop</p> <p>11 severe, chronic diarrhea, diarrhea that doesn't</p> <p>12 go away, significant weight loss, even if it</p> <p>13 happens months or years after you start taking</p> <p>14 this drug, you need to come back to me so I can</p> <p>15 evaluate whether or not the olmesartan is a</p> <p>16 factor in that.</p> <p>17 That's a reasonable</p> <p>18 recommendation that physicians tell that to</p> <p>19 patients; correct?</p> <p>20 A. I would say that the physician</p> <p>21 could tell the patient something like this:</p> <p>22 I'm going to start you on this</p> <p>23 medication because I think it's a good</p> <p>24 medication. You should be aware that there are</p>	<p style="text-align: right;">Page 68</p> <p>1 their entirety?</p> <p>2 A. I skimmed them.</p> <p>3 Q. You list in 11 and 12 deposition</p> <p>4 transcripts of Dr. Leffler and Dr. Turner.</p> <p>5 Did you read those?</p> <p>6 A. I skimmed through them.</p> <p>7 Q. As you sit here now, was there</p> <p>8 anything of any significance one way or another</p> <p>9 that you could point to in any of those materials</p> <p>10 listed from 7 to 12 that have any significant</p> <p>11 impact on your opinions as you sit here right</p> <p>12 now?</p> <p>13 MR. CHRISTIAN: Objection. Form.</p> <p>14 THE WITNESS: I think what I</p> <p>15 would say -- well, perhaps I could get a</p> <p>16 clarification. Are you wishing for me to</p> <p>17 expound upon my opinion about other</p> <p>18 people's opinion?</p> <p>19 BY MR. SLATER:</p> <p>20 Q. No, I'm not asking you to do</p> <p>21 that. Let me ask it differently.</p> <p>22 You wrote your report, which is</p> <p>23 marked -- let me go back to the report and we'll</p> <p>24 come back to this.</p>
<p style="text-align: right;">Page 67</p> <p>1 scattered case reports of some patients that</p> <p>2 develop some possible gastrointestinal side</p> <p>3 effects. So you should be aware of that, but</p> <p>4 there have never been any randomized trials to</p> <p>5 indicate that this association is a strong one or</p> <p>6 that it's anything more than rare. But if you</p> <p>7 should encounter that, yes, please let me know.</p> <p>8 That would be the appropriate --</p> <p>9 Q. Okay.</p> <p>10 A. -- thing to say.</p> <p>11 Q. Move to strike.</p> <p>12 Let's look at Exhibit 5. We were</p> <p>13 provided this last night.</p> <p>14 Are these materials that you</p> <p>15 reviewed after you wrote your initial report,</p> <p>16 which is -- well, rephrase.</p> <p>17 Looking at Exhibit 5, had you</p> <p>18 read any of these materials when you wrote your</p> <p>19 report, which we marked as Exhibit 4?</p> <p>20 A. To my recollection, I had not</p> <p>21 read these papers at the time.</p> <p>22 Q. You list in number 7, 8, 9, and</p> <p>23 10 four expert reports.</p> <p>24 Did you read those reports in</p>	<p style="text-align: right;">Page 69</p> <p>1 Exhibit 4 is your report in this</p> <p>2 case, and it's the only report that we've been</p> <p>3 provided; correct?</p> <p>4 A. Yes.</p> <p>5 Q. Does this report contain each of</p> <p>6 the opinions that you formed in this case?</p> <p>7 A. Yes.</p> <p>8 Q. During the course of the report,</p> <p>9 you discuss certain facts, mostly facts that are</p> <p>10 facts from published articles.</p> <p>11 Are those the facts you felt were</p> <p>12 most important to you in forming your opinions?</p> <p>13 A. Yes.</p> <p>14 Q. Did you carefully state each of</p> <p>15 the opinions and each -- rephrase.</p> <p>16 Did you carefully write this</p> <p>17 report in the sense that you went back and</p> <p>18 proofread it and make sure it said exactly what</p> <p>19 you want it to say before you signed it and it</p> <p>20 was sent to us?</p> <p>21 A. Yes.</p> <p>22 Q. Now, going to Exhibit 5, items 7</p> <p>23 through 12, did reading any of those items, those</p> <p>24 reports and those transcripts, change any of the</p>

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<p style="text-align: right;">Page 70</p> <p>1 opinions that are set forth in Exhibit 4, the 2 report you wrote?</p> <p>3 A. What I would -- the only way I 4 can comment on that would be to give you my 5 opinion of other people's opinion. So if you 6 would like me to do that, I can do that. If you 7 don't want me to do that, I can't answer your 8 question.</p> <p>9 Q. Not asking you to do it. 10 So my question is this: Did 11 reading those expert reports and those 12 transcripts change the opinions set forth in 13 Exhibit 4 in any way?</p> <p>14 A. I think they actually strengthen 15 my opinion because -- if you allow me to say? 16 That in the Lebowhl and Leffler 17 reports, I was rather shocked to read a lot of 18 opinion that wasn't based in fact. So it was 19 just based on sentiment or ideas of what they 20 believe and, therefore, I felt that this caused 21 me to go back and reread some of the papers out 22 of Columbia again and to think through what I had 23 written in my report. 24 And in so doing, that was why I</p>	<p style="text-align: right;">Page 72</p> <p>1 if it's written in stone. I would say different 2 doctors, based on their clinical experience, will 3 have their own opinion about whether a drug has 4 the potential to contribute to certain 5 symptomatology and they may decide, I'm never 6 going to use this.</p> <p>7 For example, endocrinologists 8 struggle with drugs for the treatment of Type 2 9 diabetes because Metformin, which is the most 10 commonly used drugs, causes a lot of GI side 11 effects. So they have to make their own decision 12 about whether to use that because about 10 13 percent of patients will get diarrhea, for 14 example. So each -- each time a doctor has to 15 make that decision based on their experience.</p> <p>16 Q. Did you hold the opinion that 17 H. pylori causes gastric cancer before there was 18 an understanding of the molecular mechanism? 19 A. So by the time I started doing 20 research on H. pylori, which was in 1994, there 21 was already an announcement by the National 22 Institutes of Health that they wanted -- the 23 title of the request for applications was that 24 they were seeking grants on H. pylori-associated</p>
<p style="text-align: right;">Page 71</p> <p>1 looked up some of the IL-15 papers because I had 2 indicated that I had strong opinions about the 3 Marietta 2015 article, and when I saw that other 4 experts were citing that in a more laudatory vein 5 than the way I appreciated that article, I 6 thought it was worth my time to look at some of 7 the primary references that were cited in the 8 introduction to the Marietta paper, and that's 9 how I came up with some of those papers about 10 IL-15, for example.</p> <p>11 Q. Can -- can you guys hear me 12 still?</p> <p>13 A. Yes. 14 MR. CHRISTIAN: Yes. 15 MS. WADHWANI: Yes. 16 BY MR. SLATER: 17 Q. Okay. Move to strike from 18 "because" forward. 19 In medicine, can it be accepted 20 that a medication causes a side effect, even if 21 you don't fully understand the molecular 22 mechanism at the molecular level for why the drug 23 causes the side effect? 24 A. So you used the word "causes" as</p>	<p style="text-align: right;">Page 73</p> <p>1 gastric cancer. 2 And the World Health 3 Organization, which is an esteemed global health 4 organization, which I assume you've heard of, had 5 already called H. pylori a class I carcinogen 6 back in, I think it was, in the late '80s or 7 early '90s, before I ever did research on it. 8 So that idea was accepted, but 9 there's many of us that are still investigating 10 molecular mechanisms, but there are some that are 11 believed to be important or already understood.</p> <p>12 Q. So if I understand your answer, 13 the causal relationship between H. pylori and 14 gastric cancer has been accepted since the 1990s, 15 even before and even up to -- rephrase. Let me 16 start over. 17 If I understand your answer, it 18 has been accepted in the medical community that 19 H. pylori causes gastric cancer since the 1990s, 20 even though up till today the molecular 21 mechanisms are not fully understood; is that 22 correct? 23 A. I would say that causation of 24 gastric cancer is complex, but H. pylori is</p>

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<p style="text-align: right;">Page 74</p> <p>1 considered an important factor in causing gastric</p> <p>2 cancer, yes.</p> <p>3 Q. And the molecular mechanisms</p> <p>4 whereby H. pylori causes gastric cancer, that has</p> <p>5 not been fully established yet. That's still an</p> <p>6 area of study; correct?</p> <p>7 A. I'd like to give -- to answer</p> <p>8 that question, I'd like to give you a specific</p> <p>9 example.</p> <p>10 So there's a --</p> <p>11 Q. I just want a yes or no answer to</p> <p>12 the question, actually, Doctor.</p> <p>13 MR. CHRISTIAN: Objection. Form.</p> <p>14 THE WITNESS: So there are</p> <p>15 specific -- there are numerous molecular</p> <p>16 mechanisms that have already been</p> <p>17 established.</p> <p>18 For example, the bacteria</p> <p>19 produces a protein that gets injected</p> <p>20 into cells that's been called CagA that's</p> <p>21 strongly linked to carcinogenesis in</p> <p>22 thousands of articles and very, very</p> <p>23 large epidemiologic studies with a</p> <p>24 hundred thousand patients, but there's</p>	<p style="text-align: right;">Page 76</p> <p>1 BY MR. SLATER:</p> <p>2 Q. I'd really just like a yes or no</p> <p>3 to my question, Doctor.</p> <p>4 A. Well, it doesn't --</p> <p>5 MR. CHRISTIAN: Objection. Form.</p> <p>6 THE WITNESS: I can't give you a</p> <p>7 yes or no answer. You need to rephrase.</p> <p>8 BY MR. SLATER:</p> <p>9 Q. All right, fine. Then don't.</p> <p>10 Don't answer the question then.</p> <p>11 MR. CHRISTIAN: Objection. Side</p> <p>12 bar.</p> <p>13 THE WITNESS: Can I have a</p> <p>14 five-minute bathroom break?</p> <p>15 MR. SLATER: Sure. Sure. Take</p> <p>16 five.</p> <p>17 THE VIDEOGRAPHER: Time now is</p> <p>18 10:34. We are going off the record.</p> <p>19 This is the end of Disk No. 1.</p> <p>20 (A brief recess was taken.)</p> <p>21 (Ms. Jasiewicz no longer</p> <p>22 present.)</p> <p>23 THE VIDEOGRAPHER: The time now</p> <p>24 is 10:46. We are back on the record.</p>
<p style="text-align: right;">Page 75</p> <p>1 still other molecular mechanisms that</p> <p>2 people like me are continuing to</p> <p>3 investigate.</p> <p>4 BY MR. SLATER:</p> <p>5 Q. Tell me if you agree with this</p> <p>6 statement:</p> <p>7 "Helicobacter pylori is the</p> <p>8 strongest risk factor for the development of</p> <p>9 gastric cancer. Although the specific mechanisms</p> <p>10 by which this pathogen induces carcinogenesis</p> <p>11 have not been fully elucidated, high-expression</p> <p>12 interleukin (IL)-1B alleles are associated with</p> <p>13 increased gastric cancer risk among</p> <p>14 H. pylori-infected persons."</p> <p>15 Is that a true statement?</p> <p>16 A. Yes.</p> <p>17 Q. So even though the specific</p> <p>18 mechanisms have not been fully elucidated, the</p> <p>19 causal connection is accepted; correct?</p> <p>20 MR. CHRISTIAN: Objection. Form.</p> <p>21 THE WITNESS: So let me give you</p> <p>22 a way to interpret that language. I</p> <p>23 don't know if that was something that I</p> <p>24 wrote or --</p>	<p style="text-align: right;">Page 77</p> <p>1 This is the beginning of Disk No. 2.</p> <p>2 BY MR. SLATER:</p> <p>3 Q. Okay. Doctor, in terms of your</p> <p>4 methodology, I just asked you about the FDA</p> <p>5 notification about olmesartan.</p> <p>6 Did you not factor in the FDA's</p> <p>7 viewpoint on this question in forming your</p> <p>8 opinions?</p> <p>9 A. No, because I don't consider that</p> <p>10 scientific evidence. That was just an update to</p> <p>11 the product insert. That was my understanding.</p> <p>12 Q. In general, did you factor in the</p> <p>13 FDA's analysis of this question in any way, or</p> <p>14 did you just limit your opinion to your</p> <p>15 evaluation of the literature?</p> <p>16 MR. CHRISTIAN: Objection. Form.</p> <p>17 THE WITNESS: No, I didn't factor</p> <p>18 in the FDA's evaluation.</p> <p>19 MR. SLATER: Laura, could you</p> <p>20 mark as the next exhibit document 3, the</p> <p>21 FDA safety -- drug safety communication?</p> <p>22 MS. PITTNER: Sure.</p> <p>23 THE REPORTER: Exhibit 8.</p> <p>24 (Document marked for</p>

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<p style="text-align: right;">Page 78</p> <p>1 identification purposes as Gutman 2 Exhibit 8.) 3 MR. SLATER: We said that's 4 Exhibit 8? 5 THE WITNESS: Yes. 6 MS. PITTNER: Yes. 7 BY MR. SLATER: 8 Q. Doctor, have you seen this 9 document before? 10 A. No, not in this form. No. 11 Q. Go to the second page, please. 12 The bottom of the page under the Data Summary, 13 second paragraph. It says that the: 14 "FDA evaluated adverse event 15 reports received by FDA's Adverse Event Reporting 16 System, published literature case series, 17 information from FDA's Mini-Sentinel pilot of the 18 Sentinel Initiative, and information from the CMS 19 Medicare database." 20 Did you see what I just read? 21 A. Yes. 22 Q. It then says: 23 "FDA's evaluation found clear 24 evidence of an association between olmesartan and</p>	<p style="text-align: right;">Page 80</p> <p>1 A. Yes. 2 Q. Were you aware of what I just 3 read to you before I just read it to you? 4 A. No. 5 Q. Okay. When you're putting 6 evidence in the scale of either yes to causation 7 or no to causation, that information I just read 8 to you would go in the side of the scale that 9 weighs towards yes for causation; correct? 10 A. It's not evidence. 11 Q. It's not evidence because you 12 define evidence only to be that information that 13 comes from randomized controlled trials and 14 controlled research; is that correct? 15 A. Not only that. I have factored 16 in the current literature which includes case 17 series. However, this is just something within a 18 document, but there's no opportunity to know 19 whether any of this was reviewed by a physician 20 or scientist. This could be just laypeople 21 sending in information. I really don't have any 22 way of knowing what any of this is. 23 Q. You don't know what was done by 24 the FDA to evaluate the information they</p>
<p style="text-align: right;">Page 79</p> <p>1 sprue-like enteropathy." 2 Do you see that? 3 A. Yes. 4 Q. Were you aware before right now 5 that the FDA's evaluation found clear evidence of 6 an association between olmesartan and sprue-like 7 enteropathy based on the review of those various 8 sources of information? 9 A. No, because the only thing I was 10 aware of was just there was a change to the 11 product insert. So I haven't seen this full 12 document. 13 Q. Okay. Move to strike after "no." 14 Go to the next page, please. It 15 says: 16 "FDA identified 23 serious cases 17 in FAERS -- that's all caps -- presenting as 18 late-onset diarrhea with significant weight loss 19 and, in some cases, with intestinal villous 20 atrophy on biopsy. All patients improved 21 clinically after discontinuation of olmesartan, 22 and a positive rechallenge was seen in 10 of the 23 cases." 24 Do you see that?</p>	<p style="text-align: right;">Page 81</p> <p>1 reference there; right? 2 A. Well, I think it's kind of 3 striking that they only cite two case series, and 4 there's certainly more literature than that. 5 Q. Move to strike. 6 What I just read to you at the 7 top of the third page, you don't know what the 8 FDA did to evaluate that data in the FAERS 9 database; right? 10 A. I do not. 11 Q. And you did not take that into 12 account in forming your opinions in this case; 13 correct? 14 A. I did not. 15 Q. Look at the middle of page 3. It 16 says in the middle of the middle paragraph: 17 "Mini-Sentinel and CMS Medicare 18 assessments of ICD-9 codes for celiac disease 19 showed that at a 2-year minimum exposure, which 20 correlates with the long latency observed in 21 literature and case reports, olmesartan users had 22 a higher rate of celiac disease diagnoses and 23 claims -- in claims and administrative data than 24 users of other ARBs."</p>

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<p style="text-align: right;">Page 82</p> <p>1 Do you see what I just read?</p> <p>2 A. Yes.</p> <p>3 Q. Did you know that before I just</p> <p>4 read it to you?</p> <p>5 A. This seems to be different than</p> <p>6 the Mini-Sentinel that I reviewed, which showed</p> <p>7 no differences.</p> <p>8 Q. In the Mini-Sentinel or data from</p> <p>9 the FDA in forming your opinions; right?</p> <p>10 A. I couldn't hear the beginning of</p> <p>11 your question.</p> <p>12 Q. You did not rely on the FDA data</p> <p>13 or data relied on by the FDA at all -- you made</p> <p>14 that clear to me before -- in forming your</p> <p>15 opinions; right?</p> <p>16 A. Well, there is one Mini-Sentinel</p> <p>17 that -- I need my Table of Contents.</p> <p>18 So I was provided the -- the June</p> <p>19 2013 FDA Mini-Sentinel report, and they have a</p> <p>20 lot of graphs and tables in there. And</p> <p>21 everything I've reviewed in there, I was not able</p> <p>22 to see anything that suggested that there was any</p> <p>23 difference between olmesartan and any other ARB</p> <p>24 or other anti-hypertensives that they looked at</p>	<p style="text-align: right;">Page 84</p> <p>1 Q. -- and the higher rate of celiac</p> <p>2 disease diagnoses? That you didn't know before I</p> <p>3 just read it to you; right?</p> <p>4 A. Yes, but that's just a sentence</p> <p>5 in a report. It's not data like I'm looking at</p> <p>6 here.</p> <p>7 Q. Move to strike from "but"</p> <p>8 forward.</p> <p>9 To the extent counsel provided</p> <p>10 you information, did you hope that they would</p> <p>11 provide you information in a fair and balanced</p> <p>12 way in the sense that they would not just give</p> <p>13 you what would be supportive of your -- of the</p> <p>14 opinion they wanted you to give, but they also</p> <p>15 give you the flip side to it if there was data on</p> <p>16 the other side?</p> <p>17 MR. CHRISTIAN: Objection. Form.</p> <p>18 THE WITNESS: Of course. Yes.</p> <p>19 MR. SLATER: Okay. Let's mark as</p> <p>20 the next exhibit the updated CV. That</p> <p>21 will be Exhibit 9.</p> <p>22 MR. CHRISTIAN: This is the one</p> <p>23 that was previously marked 4?</p> <p>24 MS. PITNER: Yeah.</p>
<p style="text-align: right;">Page 83</p> <p>1 in there.</p> <p>2 Q. Okay. To be clear, that</p> <p>3 Mini-Sentinel June 2013 you just said was</p> <p>4 provided to you, you said by -- was it provided</p> <p>5 by counsel?</p> <p>6 A. Yes.</p> <p>7 Q. Okay. You said there were a lot</p> <p>8 of graphs and tables.</p> <p>9 Did you actually interpret those</p> <p>10 graphs and tables, or are you just telling me</p> <p>11 they're there?</p> <p>12 A. I mean, I flipped through it, and</p> <p>13 I kept noticing in all of them that the graphs</p> <p>14 for olmesartan were usually lower or the same as</p> <p>15 the -- as all the other drugs. So I just kind of</p> <p>16 flipped through it, and I saw they're all showing</p> <p>17 that.</p> <p>18 Q. The information I just read to</p> <p>19 you is information you had not seen before right</p> <p>20 now; correct?</p> <p>21 A. Right.</p> <p>22 Q. About the 2-year minimum</p> <p>23 exposure --</p> <p>24 A. Yeah.</p>	<p style="text-align: right;">Page 85</p> <p>1 (Document marked for</p> <p>2 identification purposes as Gutman</p> <p>3 Exhibit 9.)</p> <p>4 BY MR. SLATER:</p> <p>5 Q. Doctor, Exhibit 9, is that your</p> <p>6 most up-to-date curriculum vitae?</p> <p>7 A. As of the date of February the</p> <p>8 20th that I indicated in the header, yes.</p> <p>9 Q. I want to ask you a question</p> <p>10 about -- well, I'm going -- let me come back to</p> <p>11 something.</p> <p>12 In the earlier question, I asked</p> <p>13 you about the FDA safety notification and a</p> <p>14 phrase in there, and you said that's not</p> <p>15 evidence. Do you remember that?</p> <p>16 A. Yes.</p> <p>17 Q. And you mean that's not the type</p> <p>18 of evidence that you are relying on to form your</p> <p>19 opinions in this case; correct?</p> <p>20 A. Correct.</p> <p>21 Q. And the only evidence you're</p> <p>22 relying on to form your opinions, it's my</p> <p>23 understanding are, is the medical literature you</p> <p>24 listed in your report; correct?</p>

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<p>1 A. Correct.</p> <p>2 Q. I want to give you a hypothetical</p> <p>3 question.</p> <p>4 I'd like to describe a patient to</p> <p>5 you who takes olmesartan. Two years after</p> <p>6 starting the drug, the patient develops severe</p> <p>7 diarrhea up to 10 times a day, dehydration, loses</p> <p>8 20 pounds over the course of a month or two, gets</p> <p>9 hospitalized, and while this person is in the</p> <p>10 hospital, their blood pressure drops down and</p> <p>11 they're taken off olmesartan.</p> <p>12 They're then discharged from the</p> <p>13 hospital and over the next month or two, the</p> <p>14 diarrhea resolves, the weight starts coming back,</p> <p>15 and there's no other change to the person's</p> <p>16 medications. There's no change to the person's</p> <p>17 diet. The only change was that the person</p> <p>18 stopped taking olmesartan.</p> <p>19 Do you understand my</p> <p>20 hypothetical?</p> <p>21 A. Yes.</p> <p>22 Q. Olmesartan would need to be in</p> <p>23 the differential diagnosis as a potential cause</p> <p>24 of the diarrhea, the dehydration, and the weight</p>	<p>1 resumed.</p> <p>2 So that I don't believe there</p> <p>3 would ever be such a hypothetical because</p> <p>4 generally if someone is hypotensive or at</p> <p>5 least evidencing hypovolemia, all their</p> <p>6 blood pressure meds are going to be held.</p> <p>7 So it's essentially impossible to</p> <p>8 assume that somebody is on -- that that's</p> <p>9 the only medication change that would</p> <p>10 have been made and that it would be a</p> <p>11 situation as you enumerate it.</p> <p>12 BY MR. SLATER:</p> <p>13 Q. Move to strike.</p> <p>14 Based on my hypothetical,</p> <p>15 olmesartan would be the likely cause of the</p> <p>16 diarrhea, the dehydration, and the weight loss;</p> <p>17 correct?</p> <p>18 MR. CHRISTIAN: Objection. Form.</p> <p>19 THE WITNESS: I can't say that</p> <p>20 because they could have had an acute</p> <p>21 virus. They could have had other GI</p> <p>22 conditions, like Crohn's disease, or a</p> <p>23 big problem that we see in hospitalized</p> <p>24 patients is what we call surreptitious</p>
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<p>1 loss; correct?</p> <p>2 A. Yes.</p> <p>3 Q. And in that patient, based on my</p> <p>4 hypothetical, olmesartan would be the likely</p> <p>5 cause based on how I set out the hypothetical for</p> <p>6 the diarrhea, the dehydration, and the weight</p> <p>7 loss; correct?</p> <p>8 MR. CHRISTIAN: Objection. Form.</p> <p>9 THE WITNESS: So I'd like to</p> <p>10 answer that by saying that I have had the</p> <p>11 benefit of reviewing two of the</p> <p>12 individual plaintiff cases, and a very</p> <p>13 strong point that I'd like to make is</p> <p>14 that there's essentially a very unlikely</p> <p>15 possibility that any patient would fit</p> <p>16 your hypothetical.</p> <p>17 Because in the cases that I</p> <p>18 reviewed, they were on numerous other</p> <p>19 medications, and most of the medications</p> <p>20 were held when they were admitted. And</p> <p>21 then when they were discharged, it was</p> <p>22 extremely difficult to determine if they</p> <p>23 were resuming their olmesartan or not and</p> <p>24 which other anti-hypertensives they</p>	<p>1 use of NSAIDs, which is patients that are</p> <p>2 taking over-the-counter nonsteroidals and</p> <p>3 don't realize that that's a medication</p> <p>4 and fail to tell the physicians about</p> <p>5 this, and that sort of thing.</p> <p>6 So you may think that that's the</p> <p>7 hypothetical scenario, but you haven't</p> <p>8 told me whether a full workup was done</p> <p>9 for seronegative celiac disease, or</p> <p>10 celiac disease, or infectious diarrhea,</p> <p>11 or parasitic diarrhea, or</p> <p>12 virally-induced, or autoimmune diarrhea,</p> <p>13 or any other type of condition.</p> <p>14 BY MR. SLATER:</p> <p>15 Q. Okay. Move to strike.</p> <p>16 Doctor, taking somebody off</p> <p>17 olmesartan would not resolve chronic diarrhea,</p> <p>18 dehydration, and weight loss if the person's</p> <p>19 symptoms were being caused by celiac disease;</p> <p>20 correct?</p> <p>21 A. Celiac disease can definitely</p> <p>22 have a waxing and waning course. So it could be</p> <p>23 that while they were in the hospital, they were</p> <p>24 taken off of any kind of gluten. Maybe they were</p>

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<p style="text-align: right;">Page 90</p> <p>1 just on IV fluids. Maybe they just got put on a 2 clear liquid diet that doesn't have gluten in it, 3 so they got better. So they could be 4 mischaracterized as having a drug-associated 5 condition; whereas, it could be that they had 6 occult celiac disease.</p> <p>7 Q. Okay. Let's assume for my 8 hypothetical the person had a full workup, was 9 not taking NSAIDs, continued to eat gluten the 10 entire time, and the diarrhea never came back 11 ever again. This severe diarrhea with 12 dehydration and weight loss, it never occurred 13 again and the person never went back on 14 olmesartan.</p> <p>15 Having added that those factors 16 in response to your question, the likely cause 17 for the diarrhea, the dehydration, and the weight 18 loss would be the olmesartan; correct?</p> <p>19 MR. CHRISTIAN: Objection. Form. 20 THE WITNESS: It could be a 21 cause. However, when you say a full 22 workup was done, you know, there's the 23 full workup done, but maybe something 24 wasn't thought of or something could have</p>	<p style="text-align: right;">Page 92</p> <p>1 It says at the end of the article 2 that there was grant support provided including 3 from the National Institutes of Health; correct?</p> <p>4 A. Yes.</p> <p>5 Q. Okay. I saw some sort of a 6 reference in your report to doubting whether this 7 was a real peer-reviewed article because it was 8 published in the Mayo Clinic proceedings.</p> <p>9 Are you testifying here under 10 oath that the Mayo Clinic did not perform a 11 proper peer review of this article in the sense 12 that they just let it slide through because these 13 were Mayo Clinic doctors, and they committed 14 academic impropriety by letting it be published?</p> <p>15 A. No.</p> <p>16 MR. CHRISTIAN: Objection. Form. 17 THE WITNESS: I'm not able to 18 testify to that.</p> <p>19 It was just speculation regarding 20 my concerns about inconsistencies within 21 the article suggesting to me that as a 22 frequent -- I've done peer review for 23 over 60 journals, and I'm an associate 24 editor for "Gastroenterology," which is</p>
<p style="text-align: right;">Page 91</p> <p>1 been missed.</p> <p>2 I mean, we often see patients 3 with diarrhea that were worked up in the 4 community, and then they get sent to a 5 tertiary medical center and a different 6 diagnosis is made.</p> <p>7 MR. SLATER: Move to strike from 8 "however" forward.</p> <p>9 Laura, let's mark Rubio-Tapia 10 2012 as the next exhibit. It's document 11 13, please.</p> <p>12 THE REPORTER: Exhibit 10. 13 (Document marked for 14 identification purposes as Gutman 15 Exhibit 10.)</p> <p>16 BY MR. SLATER: 17 Q. Doctor, you're familiar with the 18 article we've marked as Exhibit 10 titled "Severe 19 Sprue-Like Enteropathy Associated With 20 Olmesartan"; correct?</p> <p>21 A. Yes.</p> <p>22 Q. Okay. I want to go through some 23 issues in this study, and the first thing I want 24 to do is just establish.</p>	<p style="text-align: right;">Page 93</p> <p>1 the premier journal in the field.</p> <p>2 And, for example, on the number 3 of patients with abnormalities on 4 colonoscopy, there was a difference in 5 the number between the text and the 6 table, which if it had been reviewed by 7 three reviewers, there's zero chance that 8 a reviewer would not have picked up on 9 that.</p> <p>10 BY MR. SLATER: 11 Q. Okay. Move to strike after 12 "speculation."</p> <p>13 Are you challenging in any way 14 the academic bona fides of Dr. Murray?</p> <p>15 A. What was that word after 16 academic?</p> <p>17 Q. You know that term "bona fides," 18 meaning are you challenging Dr. Murray's academic 19 stature and credibility?</p> <p>20 A. So my interaction with Dr. Murray 21 was that we were a couple of times on the same 22 NIH review panel, and I thought he was quite 23 knowledgeable about celiac disease from observing 24 him there, but I had never reviewed any of his</p>

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<p style="text-align: right;">Page 94</p> <p>1 papers.</p> <p>2 And, frankly speaking, after</p> <p>3 reading this paper and some of the follow-up</p> <p>4 ones, I'm not challenging his academic</p> <p>5 credentials, but I have concerns about the</p> <p>6 quality of the publications.</p> <p>7 Q. There may be things in a</p> <p>8 publication that you have concerns about, maybe</p> <p>9 that the conclusions in the articles are;</p> <p>10 correct?</p> <p>11 MR. CHRISTIAN: You cut out</p> <p>12 during your question, Adam.</p> <p>13 BY MR. SLATER:</p> <p>14 Q. I'll just -- I'll move on.</p> <p>15 Okay. I want to talk -- ask you</p> <p>16 some questions about this study now.</p> <p>17 A. Can I just -- I would just like</p> <p>18 to make a comment because I think it's fair game</p> <p>19 because you brought this up.</p> <p>20 You mentioned that the study</p> <p>21 cited an NIH grant. So I was quite curious about</p> <p>22 that, and there's a -- there's a publicly</p> <p>23 available database where you can put in any grant</p> <p>24 number and read the abstract to that grant about</p>	<p style="text-align: right;">Page 96</p> <p>1 wasn't stated that they were all thought to have</p> <p>2 celiac disease.</p> <p>3 Q. Okay. Let's do this. I want to</p> <p>4 ask you about the subject of a dose effect.</p> <p>5 What is a dose effect? How do</p> <p>6 you define that term?</p> <p>7 A. So when we -- I think the purist</p> <p>8 way of thinking about that would be like this.</p> <p>9 Let's say I want to know whether a certain drug</p> <p>10 or chemical that is a pharmacologic agent kills</p> <p>11 cells. So what you do is, you take your cells</p> <p>12 and put them in a dish, and you make replicate</p> <p>13 wells in a dish.</p> <p>14 And then you add a dose-response</p> <p>15 of your drug, and then you assess cytotoxicity.</p> <p>16 And then you make a graph, and there's all</p> <p>17 different types of graphs you can see. Sometimes</p> <p>18 it's a straight graph on a 45-degree angle where</p> <p>19 it's a linear relationship. That's rare.</p> <p>20 Sometimes it's a situation where</p> <p>21 there's no effect, and then all of a sudden you</p> <p>22 get a lot of cytotoxicity. Sometimes you get a</p> <p>23 lot of cytotoxicity with a very low dose, and</p> <p>24 then that plateaus and continues. So that's the</p>
<p style="text-align: right;">Page 95</p> <p>1 what that grant hypothesizes and what the goals</p> <p>2 of the study are and what the specific aims are.</p> <p>3 And I reviewed that information</p> <p>4 relevant to this particular NIH grant that was</p> <p>5 cited, and that grant has absolutely nothing to</p> <p>6 do with this condition or this situation.</p> <p>7 Q. Move to strike.</p> <p>8 A. So it's not -- it's not like the</p> <p>9 NIH reviewed a plan to study this proposed</p> <p>10 indication -- proposed situation.</p> <p>11 Q. Well, what was the subject of the</p> <p>12 NIH grant?</p> <p>13 A. I don't recall exactly. I think</p> <p>14 it was something about celiac disease.</p> <p>15 Q. You know these patients were all</p> <p>16 sent to this hospital at the Mayo Clinic with</p> <p>17 diagnoses of celiac; right?</p> <p>18 You know that; right, Doctor?</p> <p>19 A. I'm not certain that that was the</p> <p>20 inclusion criteria.</p> <p>21 No. It says that "we were</p> <p>22 studying a cohort of patients with collagenous</p> <p>23 sprue." So I don't know how they found</p> <p>24 themselves going to Mayo Clinic exactly. It</p>	<p style="text-align: right;">Page 97</p> <p>1 purist example.</p> <p>2 In this study, the problem is</p> <p>3 there was no attempt to relate the severity of</p> <p>4 symptoms to the dose of the drug that the</p> <p>5 patients were taking.</p> <p>6 Q. Okay. Move to strike.</p> <p>7 Doctor, with all due respect, I</p> <p>8 didn't need that explanation. I just was asking</p> <p>9 for the definition of a dose effect.</p> <p>10 A. That's the definition.</p> <p>11 Q. A dose -- all right.</p> <p>12 A dose effect would basically</p> <p>13 correlate the amount of the drug you take to the</p> <p>14 side effect you're studying; right?</p> <p>15 A. Not necessarily a side effect.</p> <p>16 It could be an efficacy.</p> <p>17 Q. Efficacy issue. Okay.</p> <p>18 One does not need to establish a</p> <p>19 dose effect to prove causation; right?</p> <p>20 A. Well, in the Bradford Hill</p> <p>21 criteria, there's the suggestion that there</p> <p>22 should be a dose effect.</p> <p>23 Q. Understanding of the Bradford</p> <p>24 Hill criteria that each of those criteria has to</p>

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<p style="text-align: right;">Page 98</p> <p>1 be met to establish causation; is that your 2 understanding?</p> <p>3 A. I don't -- I think it's more of a 4 legal situation with the Bradford Hill criteria. 5 I think that the more criteria you have, the 6 stronger your case that there is an association.</p> <p>7 Q. Okay. Here's the question. Move 8 to strike.</p> <p>9 Do you know in application of the 10 Bradford Hill criteria whether it is necessary to 11 satisfy each criteria to prove causation? Do you 12 know?</p> <p>13 MR. CHRISTIAN: Objection. Form. 14 THE WITNESS: I don't really know 15 if you need -- so you're -- you're acting 16 like as if every criteria is a binary 17 result, and nothing in medicine is a 18 binary result.</p> <p>19 So it would be more how good is 20 the evidence for each of those criteria, 21 and then you would factor in everything 22 at the end.</p> <p>23 BY MR. SLATER: 24 Q. Move to strike after "I don't</p>	<p style="text-align: right;">Page 100</p> <p>1 simplistic a result that you're asking me 2 to answer.</p> <p>3 I think that it would be obvious 4 that if there's very poor evidence based 5 on the criteria, that you would think 6 that there wasn't causation, and if there 7 were all other the criteria were very 8 strongly met, then you would lean toward 9 saying there is causation and then it's 10 a -- it's a gradient.</p> <p>11 BY MR. SLATER: 12 Q. That's your feeling about it, but 13 you haven't actually read anything that says 14 that; right?</p> <p>15 A. I suppose not.</p> <p>16 Q. Your application of the Bradford 17 Hill criteria is based on your own personal view 18 of how to apply it, not based on having studied 19 how the Bradford Hill criteria is supposed to be 20 applied; correct?</p> <p>21 MR. CHRISTIAN: Objection. Form. 22 THE WITNESS: Yes.</p> <p>23 BY MR. SLATER: 24 Q. There can be a threshold effect</p>
<p style="text-align: right;">Page 99</p> <p>1 know."</p> <p>2 You've never applied the Bradford 3 Hill criteria specifically where you've actually 4 said, I'm applying these criteria, listed them 5 and analyzed them one by one, until you wrote 6 this report; right? This is the first time 7 you've done that; right?</p> <p>8 A. That's correct.</p> <p>9 Q. And as you sit here now, you 10 don't know whether in order to satisfy the 11 Bradford Hill criteria, as that criteria is 12 understood by people who use it, whether it's 13 necessary to satisfy each criteria to prove 14 causation. You don't know; right?</p> <p>15 MR. CHRISTIAN: Objection. Form. 16 THE WITNESS: I would say that 17 I've never seen any position paper that 18 is agreed upon in the field as to exactly 19 how many of the criteria need to be met.</p> <p>20 BY MR. SLATER: 21 Q. So the answer is you don't know; 22 right?</p> <p>23 MR. CHRISTIAN: Objection. Form. 24 THE WITNESS: I think that's too</p>	<p style="text-align: right;">Page 101</p> <p>1 with regard to, for example, gluten to cause 2 celiac where there's no dose effect; correct?</p> <p>3 A. I'm -- I don't understand your 4 question.</p> <p>5 Q. Effect as opposed to a dose 6 effect?</p> <p>7 MR. CHRISTIAN: We missed the 8 first part, Adam.</p> <p>9 BY MR. SLATER: 10 Q. Do you know the term "threshold 11 effect" as opposed to a dose effect?</p> <p>12 A. I mean, of course I'm familiar 13 with the word "threshold," and it's thrown around 14 in various types of research, but I'm not really 15 sure what a threshold effect is in relationship 16 to celiac disease.</p> <p>17 Q. There's no dose effect with 18 regard to gluten and celiac; right?</p> <p>19 A. I think there probably is.</p> <p>20 Q. Not anything in the published 21 literature for that feeling?</p> <p>22 A. I've talked to people that I know 23 who have celiac disease and asked them about that 24 and tried to get a handle on how rigorous they</p>

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<p style="text-align: right;">Page 102</p> <p>1 feel that they need to be when they have their 2 diet when they travel and such. I've been 3 interested in that exact question, and I think 4 each patient has a different experience. 5 Q. Doctor, it's a very simple 6 question. 7 Is there anything in the 8 published literature that you can point to that 9 says there is a dose effect with regard to gluten 10 and celiac disease? 11 A. So the answer is, I don't know 12 because I have not run a search on that because 13 this condition that we're discussing here is not 14 celiac disease. So it did not occur to me to 15 look at the tens of thousands of papers about 16 celiac disease and gluten. 17 Q. Do you -- 18 A. So I'm not -- 19 Q. -- realize that were not -- 20 A. So I'm not prepared -- go ahead. 21 Q. I'm sorry. Are you still 22 talking? 23 A. I'm not prepared to expound upon 24 that detailed question.</p>	<p style="text-align: right;">Page 104</p> <p>1 this is just one and, therefore, I don't think 2 you could make any binary decision based on 3 whether there's a dose effect or not. 4 Q. Okay. Am I correct that in 5 forming your opinions in this case, you did not 6 consider any analogies between celiac disease and 7 olmesartan-associated enteropathy? Am I correct 8 that's not part of your analysis? 9 A. In terms of overall causation, 10 no. In terms of when I looked at some of the 11 individual cases, I tried to ferret out whether 12 they could possibly have celiac disease. But in 13 reference to what you're asking me, the answer 14 is, I did not consider that. 15 Q. Give me one second. 16 Let's look at -- do you have your 17 report handy? 18 A. Yes. 19 Q. Exhibit 4? 20 A. Oh, well, let me. 21 Q. Please turn to page 3. 22 MR. CHRISTIAN: You can use that 23 copy if you want. 24 THE WITNESS: I can use this</p>
<p style="text-align: right;">Page 103</p> <p>1 Q. Okay. As you sit here now, you 2 don't know what the literature says in terms of 3 whether it's accepted or not that there's no dose 4 effect with regard to gluten and celiac. You 5 just don't know that answer as you sit here right 6 now; correct? 7 A. That's correct. 8 Q. One does not need a dose effect 9 to prove causality; correct? 10 MR. CHRISTIAN: Objection. Form. 11 THE WITNESS: I think it's 12 important. I can't say that that's the 13 only thing that matters. It's just one 14 of the things that I pointed out that 15 they didn't assess in this study. 16 BY MR. SLATER: 17 Q. One does not need to prove that 18 there's a dose effect between a drug and a side 19 effect to prove the drug causes the side effect. 20 That's a true statement; correct? 21 A. I think I've already answered 22 that. 23 In other words, there's multiple 24 criteria to decide if there's a relationship, and</p>	<p style="text-align: right;">Page 105</p> <p>1 copy? Mine is a little bit larger. 2 Page 3? 3 BY MR. SLATER: 4 Q. Right. You have -- you're going 5 through what you call the key points in the 6 Rubio-Tapia case series, and I want to look at 7 number 2 under Duration of Exposure. 8 Do you see where I'm looking? 9 A. Yes. 10 Q. You say, in part: 11 "The implication is that the 12 effect may be idiosyncratic since there is not 13 the cause and effect reaction seen with most drug 14 allergies." 15 Do you see what I just read? 16 A. Yes. 17 Q. Okay. So if I understand 18 correctly, you're evaluating 19 olmesartan-associated enteropathy as a drug 20 allergy; correct? 21 A. I'm considering whether it could 22 be. 23 Q. Do you agree that as described in 24 the literature, olmesartan-associated enteropathy</p>

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<p style="text-align: right;">Page 106</p> <p>1 is a long-term late-onset adverse drug reaction?</p> <p>2 A. Yes.</p> <p>3 MR. CHRISTIAN: Objection. Form.</p> <p>4 THE WITNESS: Yes.</p> <p>5 BY MR. SLATER:</p> <p>6 Q. Is there any article you can</p> <p>7 point to, any of the articles you read, that</p> <p>8 refer to olmesartan-associated enteropathy as a</p> <p>9 drug allergy?</p> <p>10 A. No.</p> <p>11 Q. And I just want to make one thing</p> <p>12 clear. I've been referring to</p> <p>13 olmesartan-associated enteropathy and I've</p> <p>14 referred to "as described in literature."</p> <p>15 Have you understood me to be</p> <p>16 talking about that term which is described</p> <p>17 variously as olmesartan-associated enteropathy,</p> <p>18 sprue-like enteropathy, olmesartan-induced</p> <p>19 enteropathy? Have you understood that we're</p> <p>20 talking about this condition in general?</p> <p>21 A. I do find it interesting that</p> <p>22 you're required to use a hand gesture that's very</p> <p>23 large, which reiterates my concern as I was going</p> <p>24 through my report, which is that it would be very</p>	<p style="text-align: right;">Page 108</p> <p>1 A. I'm not absolutely certain about</p> <p>2 that.</p> <p>3 Q. Anything right now; right?</p> <p>4 A. No, I cannot.</p> <p>5 Q. But your evaluation you</p> <p>6 believe -- rephrase.</p> <p>7 In evaluating the question you</p> <p>8 were asked to answer, you've considered</p> <p>9 olmesartan enteropathy as a drug allergy;</p> <p>10 correct?</p> <p>11 MR. CHRISTIAN: Objection. Form.</p> <p>12 THE WITNESS: So the reason that</p> <p>13 I -- the real reason why I thought to</p> <p>14 write this is that in one of the two</p> <p>15 cases that I reviewed, the follow-up</p> <p>16 notes it was indicated that that person</p> <p>17 was allergic to olmesartan.</p> <p>18 So I thought, let me look at this</p> <p>19 literature in the context of whether it</p> <p>20 would ever be considered an allergy.</p> <p>21 BY MR. SLATER:</p> <p>22 Q. The duration of exposure, the</p> <p>23 fact that the onset can be months or years even,</p> <p>24 that does not disprove causality here; correct?</p>
<p style="text-align: right;">Page 107</p> <p>1 difficult if I asked you to define the syndrome</p> <p>2 in one sentence that would be consistent with all</p> <p>3 of these case series and all of these opinion</p> <p>4 pieces. I don't think you'd be able to. So</p> <p>5 it's -- it's a very diffuse, poorly-defined</p> <p>6 syndrome.</p> <p>7 Q. All right. Move to strike.</p> <p>8 I'll just keep going.</p> <p>9 And I don't have any idea what</p> <p>10 you're talking about with the hand gestures. You</p> <p>11 thought that was some sort of an important tell?</p> <p>12 I'll tell you what, Doctor. When</p> <p>13 you're on the witness stand in front of a jury,</p> <p>14 I'll use the same hand gestures and you can make</p> <p>15 the same comment. How is that for a deal?</p> <p>16 MR. CHRISTIAN: Objection. Form.</p> <p>17 Argumentative. Side bar. Go on.</p> <p>18 BY MR. SLATER:</p> <p>19 Q. We'll do that. Okay.</p> <p>20 Doctor, there is not a published</p> <p>21 article in any peer-reviewed journal describing</p> <p>22 olmesartan enteropathy, sprue-like enteropathy,</p> <p>23 olmesartan-induced enteropathy as a drug allergy,</p> <p>24 as far as you can tell; right?</p>	<p style="text-align: right;">Page 109</p> <p>1 MR. CHRISTIAN: Objection. Form.</p> <p>2 THE WITNESS: It doesn't disprove</p> <p>3 that there could be an association.</p> <p>4 BY MR. SLATER:</p> <p>5 Q. The term "association" -- well,</p> <p>6 rephrase.</p> <p>7 When one talks about an</p> <p>8 association, there are different -- rephrase.</p> <p>9 There is a spectrum of</p> <p>10 associations from associations where you would</p> <p>11 say it's unlikely to be causal, all the way up to</p> <p>12 causal associations where you believe, yes,</p> <p>13 there's an association and it causes -- one</p> <p>14 causes the other. There's a spectrum; right?</p> <p>15 MR. CHRISTIAN: Objection. Form.</p> <p>16 THE WITNESS: I think that that's</p> <p>17 probably true.</p> <p>18 BY MR. SLATER:</p> <p>19 Q. And you agree that there is an</p> <p>20 association between olmesartan and olmesartan</p> <p>21 enteropathy as described in the literature. You</p> <p>22 just disagree that there is a causal association;</p> <p>23 correct?</p> <p>24 A. What I would say is that there</p>

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<p style="text-align: right;">Page 110</p> <p>1 are case series suggesting an association. 2 However, there are multiple negative studies that 3 I cited in my report that are higher level 4 evidence that are different than just collecting 5 cases where things were looked at in a more 6 unbiased manner, and they found no association. 7 Q. Is there any article in the 8 literature that you can point me to where the 9 conclusion of the article is that there is no 10 association between olmesartan and olmesartan 11 enteropathy? Any article where that's the 12 conclusion where they say there is no 13 association? 14 A. So I just want to double-check 15 what I'm about to say. So just give me a moment. 16 Okay. So if you look at the 17 abstract to the Greywoode article published in 18 2014 out of Columbia, they looked at 2,088 19 patients undergoing upper endoscopy and 12,428 20 patients undergoing colonoscopy, and they did a 21 multivaried analysis. Meaning they factored in 22 different criteria which, you know, I'm not 23 certain what every criteria were that they 24 included.</p>	<p style="text-align: right;">Page 112</p> <p>1 Q. So they don't conclude the 2 association doesn't exist; right? They actually 3 say it does exist, but it's probably rare? 4 A. They don't say it exists. They 5 say "recently associated with." It doesn't mean 6 that they're advocating it one way or the other. 7 Q. Doctor, look at the conclusion of 8 the article, the last page. It says: 9 "Our findings suggest that the 10 sprue-like enteropathy recently associated with 11 olmesartan is a rare event and milder 12 presentations causing diarrhea among substantial 13 numbers of outpatients are unlikely." 14 Do you see what I just read? 15 A. Yes. 16 Q. So they're calling it a rare 17 event; right? 18 A. Right. 19 Q. Next sentence. 20 Future studies should focus on 21 the mechanisms by which olmesartan causes severe 22 sprue-like enteropathy, and the identification of 23 patient-related risk factors that predispose for 24 this rare but serious outcome."</p>
<p style="text-align: right;">Page 111</p> <p>1 But they found that there was no 2 statistically significant association between 3 olmesartan and diarrhea among those undergoing 4 either type of procedure, and the review of the 5 pathology reports also showed no association. 6 And then the concluding sentence: 7 "Our findings suggest that 8 neither olmesartan nor other ARBs were associated 9 with diarrhea among patients undergoing 10 endoscopy." 11 Q. Doctor, look at the conclusion of 12 the article. 13 A. That is the conclusion. 14 Q. Actually, don't do that. Go to 15 the next sentence, actually, in the abstract. 16 Do you see the next sentence in 17 the abstract after the one you just read? 18 A. Yeah, of course I do. 19 Q. And what does that sentence say? 20 Read it for the record, please? 21 A. "The sprue-like enteropathy 22 recently associated with olmesartan is likely a 23 rare adverse effect and milder presentations are 24 unlikely."</p>	<p style="text-align: right;">Page 113</p> <p>1 Do you see that sentence? 2 A. I see that sentence. 3 Q. Do you see that the authors 4 actually are saying olmesartan causes severe 5 sprue-like enteropathy? Do you see that, that's 6 what they say -- 7 MR. CHRISTIAN: Objection. 8 BY MR. SLATER: 9 Q. -- in their conclusion? 10 MR. CHRISTIAN: Objection. Form. 11 THE WITNESS: But that is not 12 consistent with the findings of their 13 study. So it doesn't make any sense that 14 they're just referring back to other 15 people's studies at that point. 16 BY MR. SLATER: 17 Q. Doctor, move to strike. 18 Do you see that that's what the 19 sentence says? 20 A. I do, but I don't agree with it 21 because that's not the conclusion of their 22 research. 23 Q. Question, okay? 24 I'm not asking you to interpret</p>